Acute Services Division

NHS Greater Glasgow and Clyde

# Therapeutics

## A Handbook for Prescribing in Adults

2013

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# Therapeutics

## A Handbook for Prescribing in Adults

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August 2013

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## Feedback

Feedback, both good and bad is welcomed by the editorial group and will be used to inform decisions about future editions.

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# Introduction

Welcome to the sixth edition of Therapeutics: A Handbook for Prescribing in Adults. This publication is intended to meet the needs of a clinical workforce increasingly moving between sites within NHS Greater Glasgow and Clyde.

The purpose of the Handbook is to promote evidence-based prescribing which is safe, effective and cost-effective. It provides a starting point for the immediate management of many common medical conditions and situations for junior doctors (and perhaps senior doctors in areas out with their main area of expertise). It is recognised, of course, that these guidelines will not be suitable for every situation and they are not intended to be a substitute for specialist expertise and clinical judgment.

Some of the guidance in this publication is based on more detailed Clinical Guidelines which can all be found in the NHSGGC Clinical Guidelines Electronic Resource Directory, accessed via the Clinical Info section of StaffNet. Where it is known that guidelines are currently being reviewed, or are scheduled to be reviewed in the near future, we have included a statement in the corresponding Handbook guidance reflecting the possibility of change.

This edition has been extensively revised in many therapeutic areas, taking account of feedback the Editorial Group have received since the publication of the last edition in August 2012 where applicable. A list of major changes can be found on the next page.

The publication of this edition also marks the near completion of the GGC Prescribing smartphone application. The app, available for smartphones and tablet devices running the Apple iOS or Android operating systems, offers access to all the guidance in the Handbook, including any updates to guidelines. It also offers access to the gentamicin (GGC) and vancomycin adult dosing calculators, access to the GGC Adult Formulary and RSS feeds to the PostScript range of bulletins, which provide supporting information for prescribers. The app will be available to download for free from the Apple App Store and Google Play Store late summer 2013 and the launch will be announced via StaffNet and the GGC Prescribing website (www.ggcprescribing.org.uk).

Feedback, both good and bad regarding the Handbook or GGC Prescribing app is welcomed to help inform and further improve the way we bring this information resource to you. You can contact us by email ggcprescribing@ggc.scot.nhs.uk

# Summary of Major changes in Therapeutics: A Handbook for Prescribing in Adults 2013

There have been a large number of changes in this edition of the handbook, however outlined below are some of the significant changes:

- The paracetamol overdose guideline has been changed to reflect new guidance in the BNF and TOXBASE. Guidance has been divided into 3 sections, presentation < 8 hours after overdose, 8 - 24 hours, > 24 hours.
- Preparation of omeprazole IV has been changed to be in-line with the Medusa monographs used within GGC. See page 49 for further information.
- Treatment of Venous Thromboembolism now includes information on the use of rivaroxaban in both deep vein thrombosis and pulmonary embolism.
- Both the antiplatelet guideline and ACS flowchart now include guidance on the use of ticagrelor.
- Changes to the stroke section include patient referral for thrombolysis if symptom onset < 4.5 hours.
- For night sedation the treatment choice has changed, see page 171.
- In the infections section there are changes, particularly in the urinary tract infection, lower respiratory tract infection and intra-abdominal sub-sections. There are additions to the alert antibiotic list and more emphasis on checking for serious drug interactions and side effects before prescribing antibiotics.
- Information in both the gentamicin and vancomycin guidelines has been revised to reflect a more safe and stepped approach to prescribing.
- In the Antidiabetic Drugs guideline additional information on safer insulin prescribing is encapsulated in 4 key components.
- The malignant ascites guideline has been updated.

## New guidelines included:

- Assessing medicines on admission in acute patients

## Guidelines updated within the online version

Guidelines updated within the online version are highlighted thus and supercede those in the printed version issued in August 2013:

**Guideline updated dd/mm/yy**

# Good prescribing practice – General advice

This guideline provides brief guidance on good prescribing practice. See the NHSGGC Medicines Reconciliation Guideline on StaffNet for more details.

**On admission** – as soon as possible (max. within 24 hours)

- Obtain complete and accurate medication history using a minimum of two information sources in accordance with the NHSGGC Medicines Reconciliation Guideline on StaffNet.
- Resolve any discrepancies between the information sources and document clearly in the patient's medical notes.
- Complete medicine reconciliation (see page 7 for general principles to consider for each medicine patient is taking on admission).

**During admission** – before prescribing:

- See page 7, Assessing Medicines on Admission in Acute Patients, for general principles.
- Ensure each medicine is appropriate and safe for the patient by checking for allergies / sensitivities, history of adverse reactions, any factors which could affect the patient's drug handling ability (e.g. renal or hepatic impairment, drug interactions, weight), formulary status of drug (see page 10), ability to take oral medicines, compliance issues.
- Continually review the need for each drug e.g. if patient is on IV antibiotics then review daily and switch to oral therapy when clinically appropriate (see page 205 for anitibiotic IV to oral policy).
- Monitor patient for potential adverse reactions.
- Document any medication changes and the reason.

**Minimising medication incidents** – on the Kardex ensure:

- Drugs are written legibly and not abbreviated using generic drug names wherever possible **unless** there is bioequivalence issues for different formulations e.g. controlled release preparations of theophylline or lithium, then prescribe by brand as a different brand can result in ineffective therapy or toxicity.
- Drugs prescribed on a separate prescription chart e.g. warfarin, insulin, gentamicin are also prescribed on the Kardex.
- Drug frequency is clear e.g. if once weekly then strike out the 6 days when the drug is not to be administered. If a drug is to be taken 'when required' then specify the maximum frequency not to be exceeded.
- For courses of treatment the duration or review date for drug(s) is stated.
- 'Micrograms', 'nanograms', 'units' are written in full e.g. 10U insulin could be read as 100 of insulin. For liquids prescribe as 'mg' not in 'ml' as different strengths of liquids may be available.
- If a decimal point is unavoidable then the dose is carefully prescribed e.g. '0.3 mg' rather than '.3 mg' and '2 mg' rather than '2.0 mg'
- The reason for stopping a drug is stated.
- Sign and date all prescriptions – if a prescription chart is re-written then the date against each drug entry should be the date the medicine was originally prescribed, not when the prescription was re-written.

## On discharge

- As the discharge prescription is often the first communication the GP will receive regarding a patient's hospital admission, review all medicines before discharge, including any withheld during admission. For more details on discharge processes see Medicines Reconciliation Policy on StaffNet. For guidance on prescribing controlled drugs on discharge, see next page.
- Ensure patient is aware of any medication changes
- Write discharge prescriptions in adequate time to allow dispensing of the medicines. Ideally 24 hours in advance of planned discharge.
- Annotate clearly on prescription if patient receives medicines in a compliance aid device.

## Compliance aids

These are used widely but may not always suitable or appropriate for the patient. If a new compliance aid is being considered for a patient then contact your ward pharmacist / pharmacy dispensary in advance of writing the discharge prescription to discuss suitability and whether the community pharmacy can continue the service. *Assessing a patient for a compliance aid may be better done after discharge to their home environment.*

## Clinical Incidents medication incident reporting

- A clinical incident is an incident which may involve a medicine and causes harm or potentially could cause harm to a patient. Many are preventable.
- All staff (medical, nursing, pharmacy) must ensure that medicine-related incidents are reported, even near misses. This is an important part of the Quality Assurance System and a necessary component of patient care. See NHSGGC Incident Management Policy and Management of Significant Clinical Incidents Policy on StaffNet for more information.
- Use DATIX, access via StaffNet, to report all incidents. All medicine-related incidents are entered in to a database and reviewed.

# Controlled Drug Prescribing

The legislation of Controlled Drugs (CDs) in the UK has recently been changed to improve patient and staff safety in relation to CDs. It is essential that a complete audit trail for CDs, from their procurement by pharmacy to administration / supply to patients or their return to pharmacy and/or destruction, is maintained.

## CD prescription requirements

On the discharge prescription the prescriber must ensure the following:

- Prescribe the CD on a separate discharge prescription form
- The CD must also be ordered in the Ward / Department CD order book by an authorised signatory. (Check with nursing staff for local procedure).
- On the discharge prescription *the following details must be handwritten* (**N.B.** *addressograph adhesive labels not allowed*):
  - The patient's name, unit or CHI number and address.
  - The **name, strength of the drug** and **form** (tablets, mixture, vial, patch, etc.).
  - The **total quantity** of dose units (i.e. number of tablets, unit dose vials, injections, patches or volume (ml) of liquids) **in words and figures**.
  - The dose / time to be taken by the patient.
  - The date of the prescription.
  - The prescriber's signature.

For example:

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Name: | Mr A. Patient | | | | | | | | | | | |
| Address: | 1 Roadside Ave<br>District<br>Glasgow | | | | | | | | | | | |
| D.O.B. | 01/01/48 | | CHI no: DDMMYY12345 | | | | | | | | | |
| Medicine | Form | Dose | Times of administration | | | | | | | | | |
| | | | am<br>6 | am<br>8 | am<br>10 | md<br>12 | pm<br>2 | pm<br>4 | pm<br>6 | pm<br>8 | pm<br>10 | Other times |
| MST | Tabs | 50 mg | | ✓ | | | | | | ✓ | | |
| Please supply 14 (fourteen) 30 mg tablets and 28 (twenty-eight) 10 mg tablets of MST | | | | | | | | | | | | |
| DRs NAME (in capitals): THE DOCTOR<br>Signature: *The Doctor* Date: 01/08/2013 | | | | | | | | | | | | |

*Continues on next page*

### Other examples

- Sevredol 10 mg tablets: take one every four hours if required for breakthrough pain. Please supply 28 (twenty-eight) 10 mg tablets.
- Fentanyl 25 microgram/hour patch: apply one patch every 72 hours. Please supply 3 (three) 25 microgram patches.
- Morphine 50 mg subcutaneously via a syringe driver over 24 hours. Supply 10 (ten) morphine 10 mg/ml amp and 5 (five) morphine 30 mg/ml amp.

Prescribers must clearly state on the prescription the quantity to be supplied of **each different formulation**.

*The following strengths of CDs are available:*

| | |
|---|---|
| MST® (Morphine **MR)** tablets | 5 mg, 10 mg, 15 mg, 30 mg, 60 mg, 100 mg, 200 mg |
| MST® (Morphine **MR)** sachets | 20 mg, 30 mg, 60 mg, 100 mg, 200 mg |
| Sevredol® (Morphine) tablets | 10 mg, 20 mg, 50 mg |
| Morphine injection | 10 mg/ml, 15 mg/ml, 30 mg/ml |
| OxyContin® (Oxycodone **MR)** tablets | 5 mg, 10 mg, 20 mg, 40 mg |
| OxyNorm® (Oxycodone) capsules | 5 mg, 10 mg, 20 mg |
| Oxycodone liquid | 5 mg/5ml |
| Fentanyl patches | 12, 25, 50, 75, 100 micrograms |
| Diamorphine injection | 5 mg, 10 mg, 30 mg, 100 mg, 500 mg |

For further advice contact pharmacy (see Appendix 6 for details).

## CD prescribing - important notes

Take care with prescribing and ensure:

- Similar sounding drugs and standard versus modified release (MR) products are written clearly to avoid misinterpretation. Common errors occur due to confusion between:
  - Oramorph® liquid and OxyNorm® liquid
  - Morphine tablets and Morphine MR tablets
  - OxyContin® and OxyNorm®
  - Prescribe MR products by brand.
- Dose prescribed is clear:

  E.g. 'Methadone 40 ml daily' does not indicate the dose to be given.
  - On the kardex prescribe:

    'Methadone 40 mg daily'
  - On discharge prescription write as:

    'Methadone oral solution 1 mg/ml, 40 ml daily'

DATIX reports show a number of incidents where millilitres and milligrams have been confused in liquid preparations. For Oramorph® 10 mg/5 ml this can result in patients receiving double the intended dose.

# Assessing Medicines on Admission in Acute Patients

Reviewing a patient's current drug therapy on admission is important with decisions to be made by the prescriber as to whether to stop, withhold, amend, or continue any particular medicine as part of the medicines reconciliation process (see page 3 for general guidance on good prescribing and the NHSGGC Medicines Reconciliation Guideline on StaffNet for more detail). It is important to note that specialist medicines are often not included in a patient's Emergency Care Summary or GP print out (e.g. darbapoeitin, methotrexate, depot antipsychotic injections, biologics) therefore always use more than one source to verify medication history.

Below are general principles to consider and illustrative examples of issues for a select group of drugs.

**General principles to consider for each medicine the patient is taking on admission**

- Ensure you know what the drug is and why the patient usually takes it
- What impact will the medicines the patient is taking for other conditions have on the treatment for their presenting complaint? Think about interactions between individual medicines or even between medicines and conditions.
- What will be the impact of withholding / stopping medicines on the patient's condition? Will it worsen the patient's pre-existing condition?
- Do any medicines need amending on admission, either to better manage the condition that they have been admitted with or to reduce the risk of further harm?

## Examples of situations using selected medicines

Considering the principles above, it should be remembered that each individual patient and their circumstances will differ. Generalised advice for selected medicines or groups of medicines follows, but this advice needs to be considered alongside the patient's individual circumstances.

*The following examples are not an exhaustive list of medicines where such considerations are required, but simply to illustrate the principles outlined above.*

### Patients who are either nil-by-mouth or have swallowing difficulties:

Follow the principles outlined above and ensure essential medicines are continued. This may require alternate routes / formulations so check suitability of alternative and dose equivalence. For instance, not all medicines can be given enterally (e.g. most modified release preparations), some may require dose adjustment if liquid preparations are used and some interact with enteral feeds. If unsure contact your clinical pharmacist / Medicines Information (Appendix 6 for contact details).

### Long-term corticosteroids:

When infection is present, to prevent adrenal insufficiency consider doubling the steroid dose. See page 293 for further advice. However, for example, if a patient has been admitted with a GI bleed, consider the risk to benefit ratio of continuing or withholding treatment – discuss with senior medical staff.

### Drug interactions:

Always check for drug interactions with all existing therapy and when prescribing new medicines. Check BNF appendix 1 for common interactions (for general antibiotic interactions, see page 204)

and information on QT interval prolongation below. Contact your clinical pharmacist or Medicines Information (appendix 6 for contact details) if unsure how to manage an interaction or its potential significance.

### Medicines for Parkinson's disease:

Missed or significantly delayed doses can have serious adverse effects and must be avoided. An accurate history of the medicines, dose and timings and preparations should be taken. See page 196 for general information on management of nil-by-mouth patients and how to obtain a supply out of hours.

### Methadone:

Important issues to consider before prescribing - See Guideline on Drug Misusers in Hospital, page 178).

### Clozapine:

Missed clozapine doses can result in relapse of psychotic illness and should be avoided. Establish how long since patient's last dose and seek senior advice / pharmacy advice if more than 48 hours have elapsed. It should be noted that acute hospital sites do not routinely stock clozapine. Ensure supply is transferred with patient between wards / hospitals to avoid a break in treatment. For more information see PostScript Acute 6 (May 2012) on www.ggcprescribing.org.uk

### Medicines for Myasthenia Gravis:

Missed / delayed doses of pyridostigmine can have serious adverse events and must be avoided; if nil-by-mouth consider nasogastric administration or parenteral neostigmine (seek pharmacy / neurology advice). Some medicines may worsen myasthenia and should be avoided e.g. gentamicin (search for 'Medicines that may affect patients with myasthenia gravis' on StaffNet). Do not alter immunosuppressants (seek advice).

### Medicines that can prolong the QT interval:

Be aware of the large number of drugs (and combination of drugs) which can prolong the QT interval. Some drugs can have a dose dependent effect, for example, see page 172 for information on citalopram. Further information on drugs and QT interval prolongation can be found in PostScript Extra 21 (www.ggcprescribing.org.uk) and www.qtdrugs.org

### Nephrotoxic drugs:

Nephrotoxic drugs (e.g. non-steroidal anti-inflammatory drugs (NSAIDs), angiotensin converting enzyme inhibitors) should be withheld in patient's presenting with an acute kidney injury. Consider restarting if renal function improves. Permanent discontinuation or a dose adjustment may be required depending on the individual circumstances. See renal advice if unsure.

### Immunosuppressant and chemotherapy agents:

Oral anticancer medicines, including chemotherapy and biological modifiers, should be withheld in all circumstances until advice is sought from the on-call haematology or oncology registrar.

Common toxicity from systemic anti-cancer treatment includes myelosuppression, vomiting, diarrhoea and mucositis though side-effects are numerous and drug–specific.

Contact local rheumatology department regarding patients on Disease Modifying Anti-Rheumatics Drugs (DMARDS) or biologics (see page 314 for list of agents) before deciding to withhold immunosuppressants.

For transplant patients, discuss with consultant before deciding to withhold immunosuppressants.

## Antiplatelets and anticoagulants:

In most cases you would not consider prescribing both an antiplatelet and an oral anticoagulant for a patient, unless on the advice of a specialist as this combination is associated with a significantly higher major haemorrhage complication rate than either agent alone. If a patient is admitted on anticoagulants, ensure the dose is clarified with a reliable source e.g. anticoagulation dosing letter (available via Clinical Portal) or the patient themselves. When starting any new medicines check for interaction with anticoagulants.

# NHSGGC Adult Formulary

**www.ggcprescribing.org.uk**

NHS Greater Glasgow and Clyde aim to promote high-quality, cost-effective prescribing in all areas of care. This Therapeutics Handbook is one such tool for prescribers to help ensure that they are consistently giving patients evidence-based treatment.

Good prescribing dictates that the choice of therapy should be made on the basis of sound clinical evidence of efficacy, safety and also takes into consideration patient acceptability and cost-effectiveness.

The Greater Glasgow and Clyde Adult Formulary takes the above into account when considering a medicine for inclusion and therefore prescribing from the Formulary is consistent with good clinical practice.

All medicines referred to in this handbook are included in the NHSGGC Adult Formulary.

## Structure of the Formulary

The NHSGGC Formulary contains two main sections, the Preferred List and the Total Formulary.

The Preferred List is composed of approximately 350 medicines which represent the first-line agents for many classes of medicine and cover many common conditions and diseases. It is primarily aimed at the generalist prescriber, and those specialists prescribing outwith their specialty. For that reason, various therapeutic areas are not suitable for inclusion in the Preferred List, for example oncology medicines.

The Total Formulary comprises all other Formulary medicines and generally contains specialist medicines and second and third-line agents from classes included in the Preferred List.

## Non-Formulary prescribing and processes

The need for prescription of medicines from out with the Formulary (non-Formulary prescribing) is recognised, but it is expected that:

- Formal treatment guidelines / protocols will exclude non-Formulary drugs.
- Non-Formulary status will apply to new medicines until accepted by the Scottish Medicines Consortium (SMC) and the Area Drug and Therapeutics Committee (ADTC). Further information regarding the SMC, including all previous decisions, can be found on their website: www.scottishmedicines.org.uk
- Non-Formulary prescribing may be necessary and approved in **exceptional** circumstances only for individual patients.
- If a non-Formulary prescription is proposed in the best interests of an individual patient, existing non-Formulary processes should be followed.

There are agreed non-Formulary processes in place within both the acute and primary care sectors of the health board. Within acute sites, there are three categories of non-Formulary prescribing / medicines. The processes that need to be followed for each category differ.

### Level 1 Non-Formulary Medicines

Most non-Formulary prescribing is monitored retrospectively using pharmacy system data and no action is required from the prescriber.

### Level 2 Non-Formulary Medicines

Whilst it is impractical for an Individual Patient Treatment Request (IPTR) form to be completed for all

non-Formulary medicines, a completed form is requested for a small number of medicines medicines that are not recommended for use by the SMC. These medicines can be found on the IPTR list available on the GGC Prescribing website www.ggcprescribing.org.uk
The treating consultant will need to complete an IPTR 2 form when a supply is required from hospital pharmacy and approval by the relevant clinical director needs to be sought prior to requesting the supply.

### Level 3 Non-Formulary Medicines

These medicines, along with level 2 medicines, can be found on the IPTR List, and because they are not recommended by the SMC, they require the more detailed IPTR3 form to be completed by the consultant and use authorised by a directorate-level IPTR panel prior to being supplied by pharmacy.

The processes listed above for IPTR 2 and 3 are current at the time of printing but may be subject to review later in 2013. Information on any changes can be found on the GGC Prescribing website: www.ggcprescribing.org.uk

The information obtained from the non-Formulary processes are collated by the Formulary Team and are used to inform ADTC and its sub-committees and individual directorates about trends regarding non-Formulary prescribing that need addressing.

## Where to find Formulary information

The Greater Glasgow and Clyde ADTC has a website containing useful Formulary information at: www.ggcprescribing.org.uk

Alternatively, the Formulary Team (see Appendix 6 for contact details), based within the Area Medicines Information Centre in Glasgow Royal Infirmary, are happy to answer any specific queries where the information is not readily available.

# Unlicensed Medicines

No medicine can be placed on the market without a Marketing Authorisation (formerly known as a Product Licence) granted by the Medicines and Healthcare Products Regulatory Authority (MHRA). This Marketing Authorisation signifies that the medicine concerned meets the appropriate quality standards and is safe and efficacious for its designated use. However, fully licensed products will not always meet the clinical needs of an individual patient in every situation. Therefore, the legislation provides an exemption to allow the manufacture, supply and administration of unlicensed medicines (i.e. medicines without a Marketing Authorisation) when necessary. In addition, provision is also made for licensed medicines (i.e. medicines with full Marketing Authorisation) to be prescribed for unlicensed indications, in unlicensed dosages or in unlicensed formulations i.e. “off-label”.

The following issues must be considered before prescribing an unlicensed / off-label medicine:

- Unlicensed Medicines and off-label medicines should only be prescribed if their use can be clearly justified from a clinical / pharmaceutical perspective.
- Products with the appropriate Marketing Authorisation should be used to treat patients in preference to unlicensed medicines or off-label use whenever possible. However, use of unlicensed / off-label medicines may be necessary in order to provide the optimum treatment for patients.
- The decision to prescribe unlicensed medicines may only be made by a consultant.
- Any practitioner prescribing an unlicensed medicine or a licensed medicine for an unlicensed indication must take responsibility for their actions. The prescriber carries the burden of the patient’s welfare and in the event of adverse reactions may be called upon to justify the decisions that they have taken.
- Appropriate documentation must be completed by the responsible consultant before an unlicensed medicine or a high risk off-label medicine is prescribed as per NHSGGC Unlicensed Medicines (ULM) Policy. Clinical pharmacists can advise further on the process and when forms need to be completed.
- Suitable patient information should be provided and informed consent obtained for patients prescribed unlicensed medicines.
- Appropriate arrangements must be made for continuity of supply when a patient is required to continue to take an unlicensed medicine after their discharge from hospital (see Policy for more details).
- The full policy together with the appropriate forms and some frequently asked questions can be found within the medicines policies section of the GGC Prescribing website at www.ggcprescribing.org.uk

# Quick guide to using the handbook

## What sort of guidance is included and excluded?

The Editorial Group has agreed criteria to determine if guidance is suitable for inclusion in the Handbook. Generally, the guidance should relate to the therapeutic management of a condition where drug therapy or other therapeutic interventions (e.g. non-invasive ventilation) are detailed. However, guidelines which simply describe practical diagnostic procedures with no therapeutic component (e.g. lumbar puncture) are not included.

### Format of guidance

Each guideline gives general information on the initial management of a clinical condition. These recommendations have been agreed by relevant specialists across NHSGGC and every effort has been made to ensure that they are complete and up to date at the time of going to print. Where appropriate, users are referred to other guidelines (or full versions of guidelines) that they may wish to consult. Most guidelines follow a standard template. The drug aspect has been highlighted in colour to allow users to easily navigate through the guideline.

### Active links in this publication

This handbook contains interactive content and index pages (click on the required page number in these sections) together with links to sites mentioned in the text – these are highlighted

### Abbreviations

The following are the most common ones which have been used in the course of the handbook:

ABG ..... Arterial Blood Gases

AVPU ..... Alert, Voice, Pain, Unresponsive

BP ..... Blood Pressure

CrCl ..... Creatinine Clearance

CRP ..... C Reactive Protein

CXR ..... Chest X-ray

ECG ..... Electrocardiogram

ESR ..... Erythrocyte Sedimentation Rate

eGFR ..... estimated Glomerular Filtration Rate

FBC ..... Full Blood Count

GCS ..... Glasgow Coma Scale

Hb ..... Haemoglobin

LFTs ..... Liver Function Tests

LVF ..... Left Ventricular Failure

RR ..... Respiratory Rate

STEMI ..... ST Elevation Myocardial Infarction

*Continues on next page*

U&Es ..... Urea and Electrolytes

WCC ..... White Cell Count

Other abbreviations used have been explained in the guidelines they are used.

## And finally

It is important to note that the final responsibility of prescribing lies with the prescribing clinician. If there are any concerns about the appropriateness of a particular treatment, seek additional and/or alternative sources of information. In addition, some specialists units have specific guidelines and these should be followed.

# Sections

1. Resuscitation and Anaphylaxis

2. Drug overdose and Toxicity

3. Gastrointestinal System

4. Cardiovascular System

5. Respiratory System

6. Central Nervous System

7. Infections

8. Endocrine System

9. Electrolyte Disturbances

10. Musculoskeletal and Joint Disease

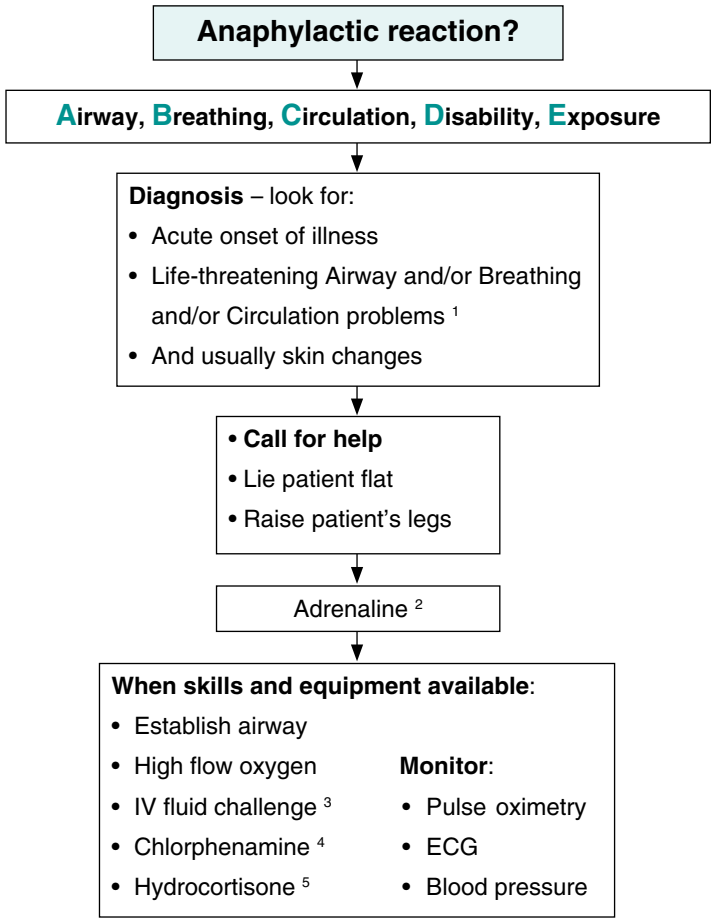
11. Palliative Care

12. Oncological Emergencies

Section 1

# Resuscitation and Anaphylaxis

# Management of Anaphylaxis




**1. Life-threatening problems**:

| | |
|---|---|
| **Airway**: | swelling, hoarseness, stridor |
| **Breathing**: | rapid breathing, wheeze, fatigue, cyanosis, $SpO_2$ < 92%, confusion |
| **Circulation**: | pale, clammy, low blood pressure, faintness, drowsy / coma |

*Continues on next page*

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**2. Adrenaline *(give IM unless experienced with IV adrenaline)***

**IM doses of 1:1000 adrenaline (repeat after 5 min if no better)**

- **Adult 500 micrograms IM (0.5 ml)**
- **Child more than 12 years: 500 micrograms IM (0.5 ml)**
- **Child 6 - 12 years: 300 micrograms IM (0.3 ml)**
- **Child less than 6 years: 150 micrograms IM (0.15 ml)**

**Adrenaline IV to be given *only by experienced specialists.***

**Titrate:** **Adults 50 micrograms; Children 1 microgram/kg**

**3. IV fluid challenge:**

**Adult – 500 - 1000 mL**

**Child – crystalloid 20 mL/kg**

**Stop IV colloid if this might be the cause of anaphylaxis.**

| | 4. Chlorphenamine (IM or slow IV) | 5. Hydrocortisone (IM or slow IV) |
|---|---|---|
| Adult or child > 12 years | 10 mg | 200 mg |
| Child 6 - 12 years | 5 mg | 100 mg |
| Child 6 months - 6 years | 2.5 mg | 50 mg |
| Child < 6 months | 250 micrograms/kg | 25 mg |

*Anaphylaxis algorithm reproduced with the kind permission of the Resuscitation Council (UK)*

## Other information

Anaphylaxis can be precipitated by a broad range of triggers which can include medicines, food, radio-opaque dyes and venom. On admission, known allergies must be clearly documented on the patient's kardex and in the medical notes. Any new allergies identified must be documented and communicated to the patient and the patient's GP. If a drug is the trigger then also complete a 'Yellow card' adverse drug reaction form. Forms can be found in the BNF or at www.yccscotland.scot.nhs.uk/

*The above algorithm has been taken from the guideline on Emergency Treatment of Anaphylactic reactions: Guidelines for healthcare providers, January 2008 (www.resus.org.uk/pages/reaction.pdf).*

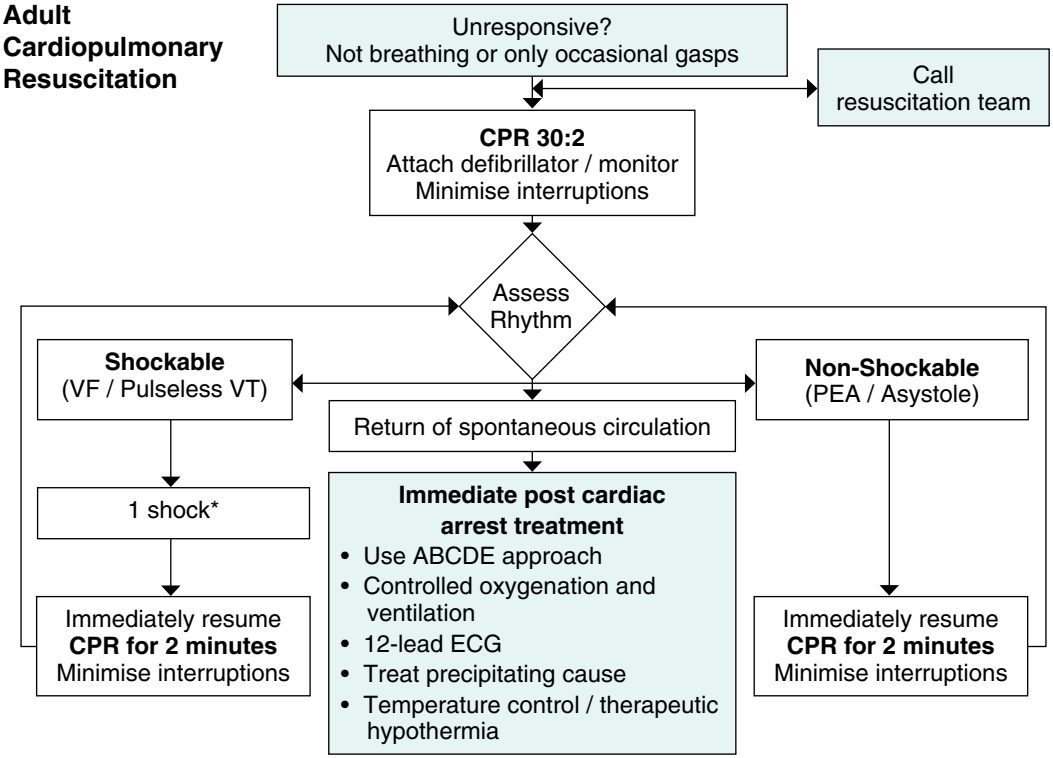
# Cardiopulmonary Resuscitation

**Note:** Under no circumstances should the emergency team enter MRI (Magnetic Resonance Imaging) areas.

Refer to the document "Cardiac Arrests or Serious Medical Emergencies Occurring in MRI Areas" available by contacting Resuscitation Officer or on StaffNet:

StaffNet / Acute / Emergency Care and Medical Services / Resuscitation / Downloads.

**Adult Cardiopulmonary Resuscitation**




**During CPR**

- Ensure high-quality CPR: rate, depth, recoil
- Plan actions before interrupting CPR
- Give oxygen
- Consider advanced airway and capnography
- Continuous chest compressions when advanced airway in place
- Vascular access (intravenous, intraosseous)
- Give adrenaline every 3 - 5 minutes
- Correct reversible causes

**Reversible Causes**

- Hypoxia
- Hypovolaemia
- Hypo- / hyperkalaemia / metabolic
- Hypothermia
- Thrombosis – coronary or pulmonary
- Tamponade – cardiac
- Toxins
- Tension pneumothorax

*Select 150 - 200 J biphasic for first shock and 150 - 360 J biphasic for subsequent shocks if required.

*Reproduced with the kind permission of the Resuscitation Council (UK)*

# Peri-arrest Arrhythmias

## General advice

Assessment and treatment of all arrhythmias should address two factors: the condition of the patient (stable versus unstable) and the nature of the arrhythmia.

### Adverse signs

The presence or absence of adverse signs or symptoms will dictate the appropriate treatment for most arrhythmias. The following adverse factors indicate that a patient is unstable because of the arrhythmia:

**Clinical evidence of low cardiac output**

Pallor, sweating, cold, clammy extremities (increased sympathetic activity), impaired consciousness (reduced cerebral blood flow), and hypotension (e.g. systolic blood pressure < 90 mmHg).

**Excessive tachycardia**

Very high heart rates (e.g. > 150 beats/min) reduce coronary blood flow and can cause myocardial ischaemia. Broad-complex tachycardias are tolerated by the heart less well than narrow-complex tachycardias.

**Excessive bradycardia**

This is defined as a heart rate of < 40 beats/min, but rates of < 60 beats/min may not be tolerated by patients with poor cardiac reserve.

**Heart failure**

Pulmonary oedema indicates failure of the left ventricle, and raised jugular venous pressure and hepatic engorgement indicate failure of the right ventricle.

**Chest pain**

The presence of chest pain implies that the arrhythmia, particularly a tachyarrhythmia, is causing myocardial ischaemia.

### Treatment options

Having determined the rhythm and presence or absence of adverse signs, there are broadly three options for immediate treatment:

- Anti-arrhythmic (and other) drugs
- Attempted electrical cardioversion
- Cardiac pacing.

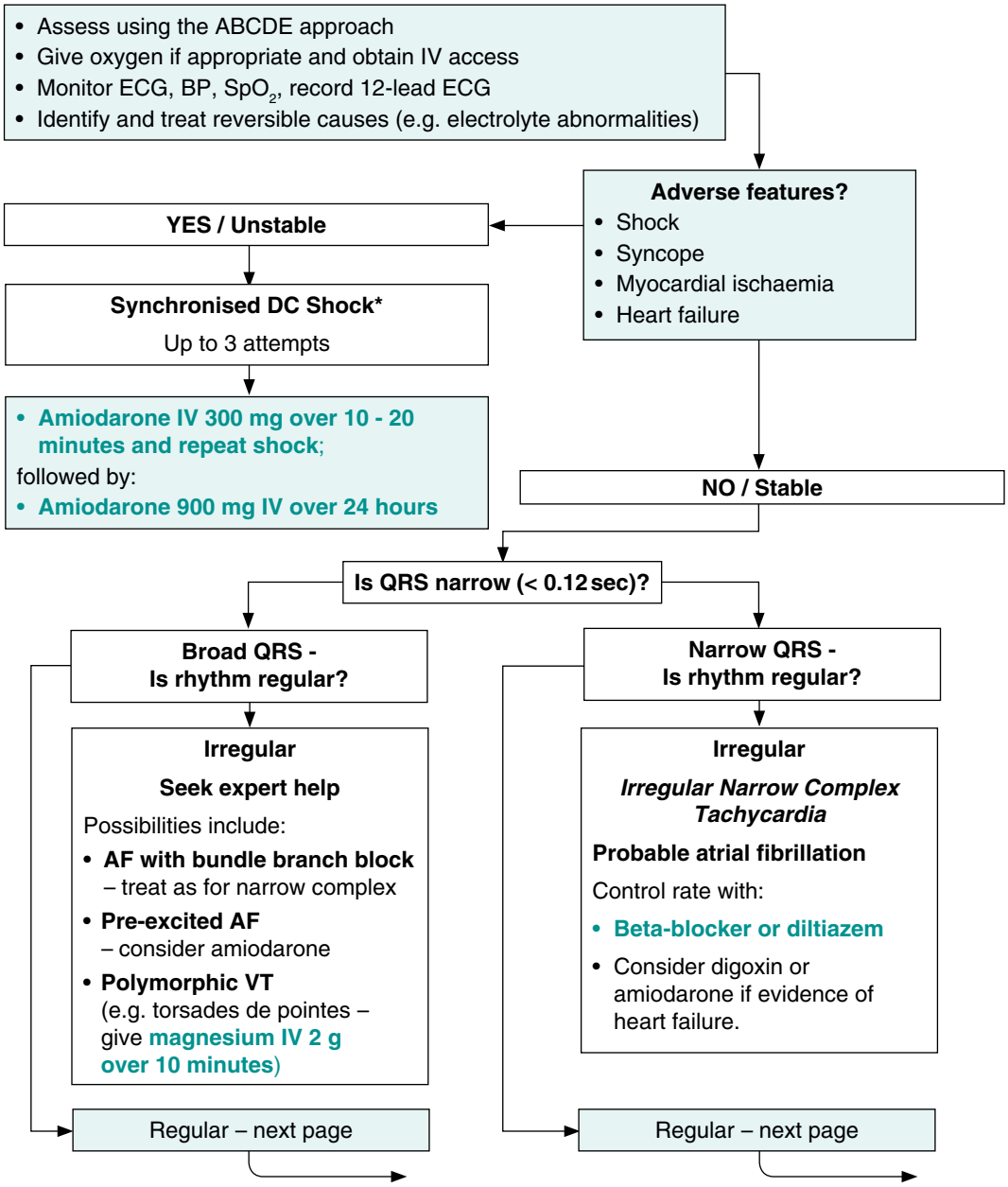
Anti-arrhythmic drugs act more slowly and less reliably than electrical cardioversion in converting a tachycardia to sinus rhythm. Thus, drugs tend to be reserved for stable patients without adverse signs, and electrical cardioversion is usually the preferred treatment for the unstable patient displaying adverse signs.

Once an arrhythmia has been treated successfully, repeat the 12-lead ECG to enable detection of any underlying abnormalities that may require long-term therapy.

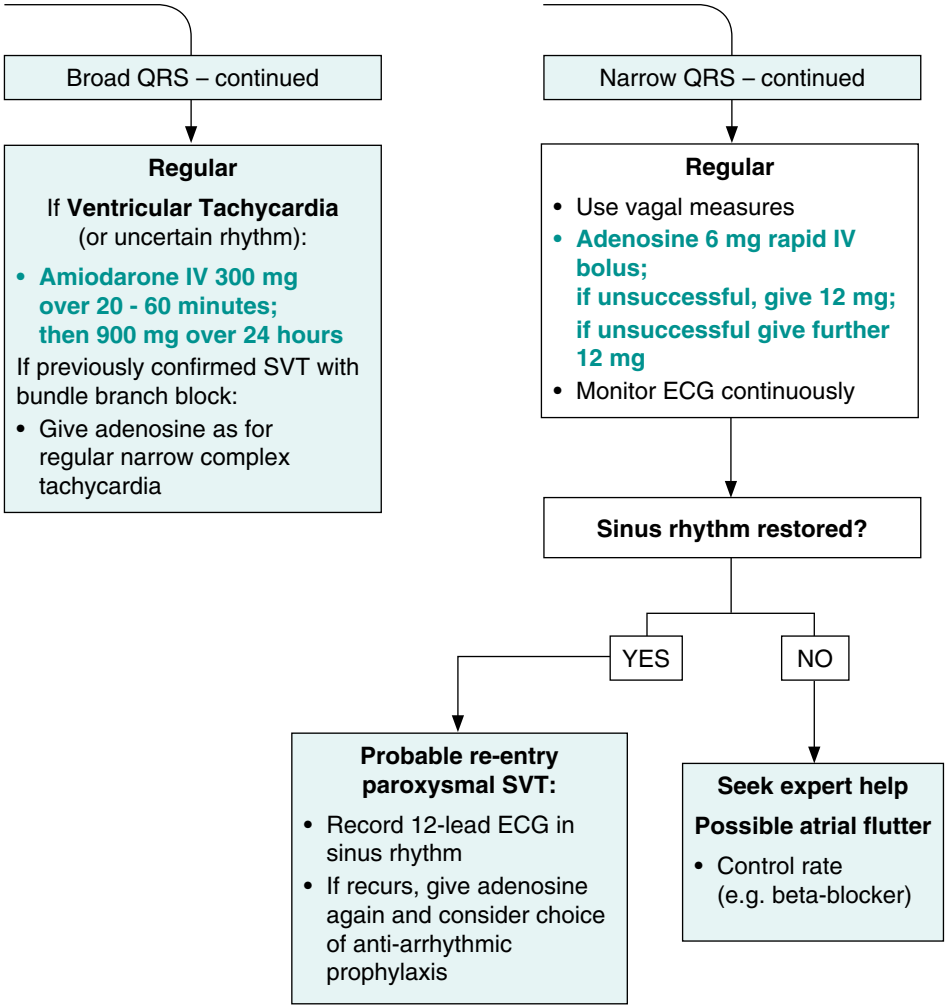
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# Tachycardia – treatment algorithm (with pulse)

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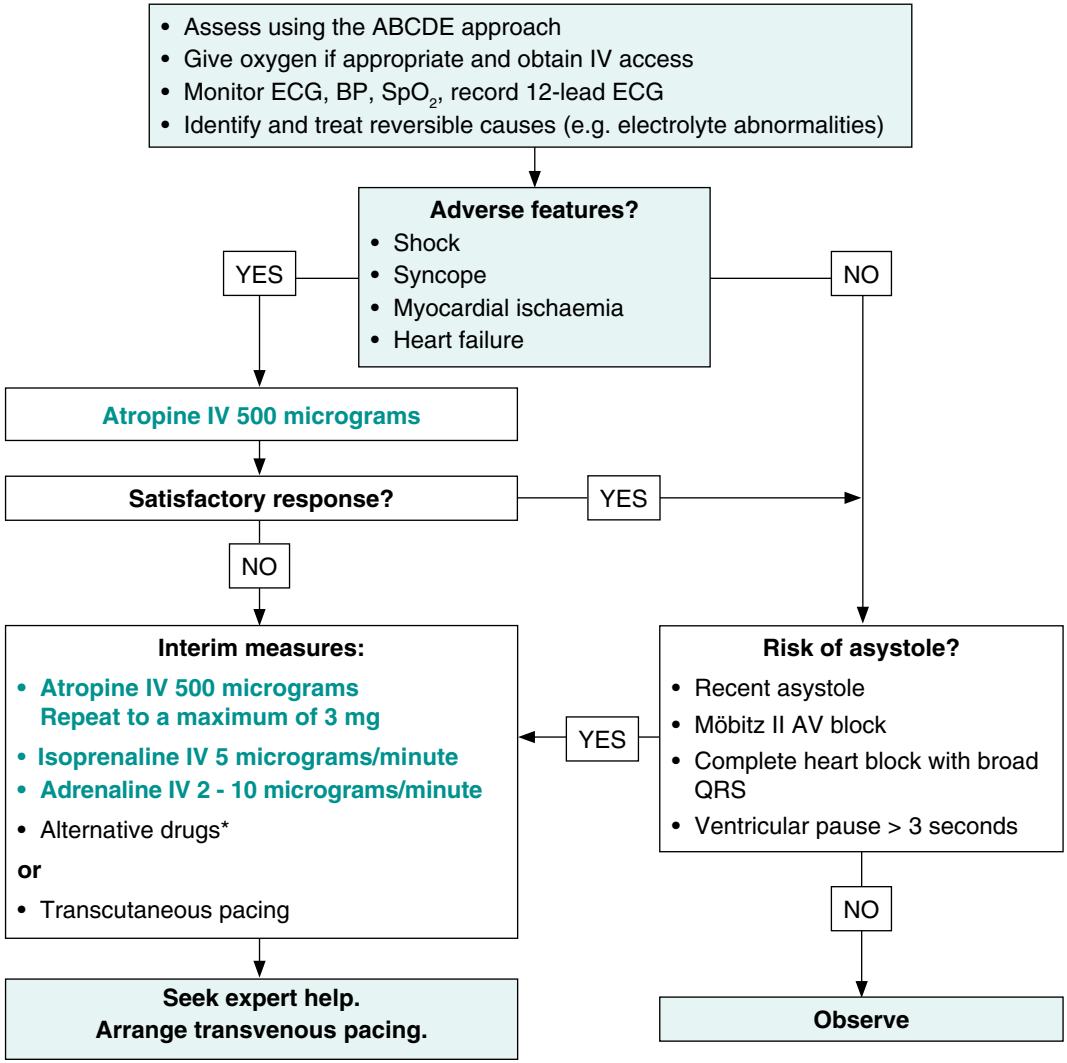



*Attempted electrical cardioversion is always undertaken under sedation or general anaesthesia.


Broad QRS – continued
Regular
If Ventricular Tachycardia (or uncertain rhythm):
• Amiodarone IV 300 mg over 20 - 60 minutes; then 900 mg over 24 hours
If previously confirmed SVT with bundle branch block:
• Give adenosine as for regular narrow complex tachycardia
Narrow QRS – continued
Regular
• Use vagal measures
• Adenosine 6 mg rapid IV bolus; if unsuccessful, give 12 mg; if unsuccessful give further 12 mg
• Monitor ECG continuously
Sinus rhythm restored?
YES
NO
Probable re-entry paroxysmal SVT:
• Record 12-lead ECG in sinus rhythm
• If recurs, give adenosine again and consider choice of anti-arrhythmic prophylaxis
Seek expert help
Possible atrial flutter
• Control rate (e.g. beta-blocker)

# Bradycardia – treatment algorithm

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*** Alternatives include:**
Aminophylline
Dopamine
Glucagon (if beta-blocker or calcium-channel blocker overdose)
Glycopyrrolate can be used instead of atropine

# Guidelines on Blood Transfusion

This guideline promotes best practice regarding blood use. Further information on blood transfusion, including details regarding sampling, administration, blood products and management of reactions is available on StaffNet by searching 'Blood Transfusion Information'.

## Indications for transfusion

### Acute blood loss

An acute blood loss of greater than 20% of blood volume (about 1000 ml blood) will often need a transfusion. Do not delay ordering blood in situations where blood loss is acute and rapid.

If blood loss is very rapid, follow the site specific protocol for dealing with major haemorrhage (also see page 27).

### For surgical patients

**Consider transfusion if:**

- Post-operative Hb falls below 80 g/L (8 g/dL).
- Pre-operative Hb is less than 90 g/L (9 g/dL) and the surgery is associated with the probability of significant blood loss, but see point below.
- Pre-operative anaemia **must** be investigated, as medical management may be more appropriate than transfusion.
- Seek to maintain Hb above 80 g/L (8 g/dL) (consideration of above 100 g/L [10 g/dL] in patients with significant comorbidity e.g. age over 70, ischaemic heart disease, valvular heart disease and peripheral vascular disease).

### Anaemia in active myocardial infarction

**(Hb below 100 g/L [10 g/dL]):**

Transfusion to an Hb of 100 g/L (10 g/dL) is desirable but to overshoot to 110 g/L (11 g/dL) may be excessive. Evaluate effect of each unit as it is given.

### Anaemia in other patients

Some anaemias will respond to treatment of deficiency e.g. iron, B12, folate. Always consider cause before transfusing.

**Hb below 80 g/L (8 g/dL):**

Consider transfusion, but evaluate after each unit.

**Hb between 80 g/L and 100 g/L (8 - 10 g/dL) and normovolaemic patients:**

Consider transfusion only if they have symptomatic anaemia or significant comorbidity.

**Symptoms and signs of anaemia include:**

- Shortness of breath for no other reason
- Angina
- Syncope
- ST depression on ECG
- Tachycardia for no other reason

*Continues on next page*

Transfusion to an Hb above 100 g/L (10 g/dL) is rarely indicated and the reason must be documented.

## Important note

- Think before transfusion. Blood is a biological product and sometimes is in short supply. Transfusions come with the potential for known and unknown risks.
- Reassess after each unit is given. Do you need to give more?
- Stop if symptoms / signs shown above resolve.
- Stop if you have reached an adequate Hb i.e. above 80 g/L (8 g/dL) in symptomless patients (100 g/L [10 g/dL] in acute MI).

# Management of Major Haemorrhage

(See site specific information on page 29)

## Introduction

The therapeutic goal in the management of massive haemorrhage is maintenance of tissue perfusion and oxygenation by restoration of blood volume and haemoglobin (see site specific information on page 29).

### Definition of major haemorrhage

Definition of acute massive haemorrhage varies. It can be defined as a 50% blood loss within 3 hours or a rate > 150 ml/minute.

The normal human blood volume in an adult is 65 - 70 ml/kg; therefore a 70 kg male has a blood volume of approximately 5000 ml – a 50% loss is approximately 2500 ml.

**1. Assess: Is this major haemorrhage? (See definition above)**

**2. Restore circulating volume**

- Wide bore peripheral cannula
- Adequate volume of crystalloid or colloid, warmed if possible
- Give oxygen and start monitoring
- Aim for BP at appropriate level

**3. Summon Help (See site specific information on page 29 - 31)**

Seek senior staff assistance:

- Surgical?
- Anaesthetics?
- ITU?
- Obstetric?
- Emergency medicine?

**4. Stop bleeding**

Consider early surgical, obstetric or interventional radiology involvement.

**5. Send blood samples**

- 6 unit crossmatch
- FBC and clotting screen including fibrinogen
- Biochemistry including calcium
- Ensure correct labelling of samples
- Consider requirement for ABGs

**6. Give blood products as appropriate (see next page)**

*Continues on next page*

# Blood products

| Blood product | Important information |
|---|---|
| Red cells | • Aim Hb > 80 g/L (8 g/dL)<br>• O neg from Blood Bank or satellite fridges (see next page for details)<br>• Group specific 25 minutes<br>• Full crossmatch 60 minutes |
| Clotting factors | • FFP: aim for PT and APTT < 1.5 x control<br>and/or<br>• Cryoprecipitate: aim fibrinogen > 1 g/L |
| Platelets | • Aim > 80 x $10^9$/L, > 100 x $10^9$/L if multiple or CNS trauma<br>• Stocks held at Gartnavel so take > 1 hour to arrive |

## In Massive Transfusion remember:

Allow *at least*:

- 20 minutes for thawing of plasma products
- 25 minutes for group specific red cells
- Up to 60 minutes for full crossmatch
- Transport time

# Other information

- If O neg used please inform Haematology / Blood transfusion lab as soon as possible to ensure replacement of units.
- Avoid wastage of blood products – return blood immediately to the Blood Transfusion lab if not being used.
- Packed red cells should not be lying out of fridge for more than 30 minutes.
- Once situation resolved inform lab staff and porters to allow them to stand down.
- Once cycle completed review clinical situation.
- Tranexamic acid – This has recently been shown to safely reduce the risk of death in bleeding trauma patients (CRASH 2 Trial). Dose is:

  **Tranexamic acid IV 1 g over 10 minutes, then infusion of 1 g over 8 hours**

*Continues on next page*

# Hospital Specific Information on Massive Haemorrhage Management

| Royal Alexandra Hospital | | | |
|---|---|---|---|
| Phone numbers | Blood storage<br>(O Neg Blood) | Key personnel | Coagulation factors |
| Call switchboard 2222 and state “Major Haemorrhage”, name of hospital and location. | Theatre Fridge, Maternity Fridge (4 units). | On-call Haematology BMS.<br>Porter via 2222 call. | Issued after discussion with on-call Haematology BMS or Haematology medical staff. |
| **Inverclyde Royal Hospital** | | | |
| Phone numbers | Blood storage<br>(O Neg Blood) | Key personnel | Coagulation factors |
| Call switchboard 2222 and state "Major Haemorrhage", name of hospital and location. | Transfusion Laboratory, Haematology Department, Level C.<br>Out-of-hours satellite fridge opposite Transfusion Office (2 units), Theatre fridge (2 Units). | On-call Haematology BMS via switchboard. | Issued after discussion with on-call Haematology BMS or Haematology medical staff. |
| **Vale of Leven Hospital** | | | |
| Phone numbers | Blood storage<br>(O Neg Blood) | Key personnel | Coagulation factors |
| Call Blood Transfusion Laboratory extension 27502. | On-call Haematology BMS via switchboard, Transfusion Laboratory.<br>Out-of-hours satellite fridge in medical assessment unit (2 units). | On-call Haematology BMS via switchboard. | Issued after discussion with on-call Haematology BMS via switchboard or Haematology medical staff. |
| **Stobhill ACH** | | | |
| Phone numbers | Blood storage<br>(O Neg Blood) | Key personnel | Coagulation factors |
| No Blood Bank on site. Call switchboard 2222 and state "Major Haemorrhage Stobhill ACH" and location, including local extension number. Call Blood Bank 24666 / 25047 | ACH Laboratory satellite fridge - 6 units. | On-call Haematology BMS via switchboard.<br>Call switchboard and request an emergency taxi to take any samples to GRI Blood Bank. | Issued after discussion with Haematology medical staff, guided by clotting results. |

Table continues on next page

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| **Southern General Hospital** | | | |
|---|---|---|---|
| Phone numbers | Blood storage<br>(O Neg Blood) | Key personnel | Coagulation factors |
| Call 2222 and state "Major Haemorrhage", name of hospital and location. | Blood Bank 61597.<br>General theatres (4 units).<br>INS theatre (2 units).<br>Labour suite (2 units.)<br>Main blood bank (2 units). | On-call Haematology BMS page 7602. | Blood Bank will automatically thaw 4 units of FFP. Further units issued once clotting screen received in lab and discussion with medical staff. |
| **Victoria Infirmary** | | | |
| Phone numbers | Blood storage<br>(O Neg Blood) | Key personnel | Coagulation factors |
| Call switchboard 2222 and state "Major Haemorrhage", name of hospital and location.<br>For ACH also call 5555 for Porter. | Blood transfusion lab Main theatre – Level E (2 units).<br>ACH fridge (2 units). | On-call Haematology BMS page 6645. | Blood Bank will automatically thaw 4 units of FFP. Further units issued once clotting screen received in lab and discussion with medical staff. |
| **Western Infirmary** | | | |
| Phone numbers | Blood storage<br>(O Neg Blood) | Key personnel | Coagulation factors |
| Call switchboard - 2222 and state "Major Haemorrhage", name of hospital and location. | WIG Level 5 fridge (3 units).<br>WIG Level 2 Theatre (6 units).<br>WIG Blood Bank. | Blood Bank, Porters, Anaesthetist are informed by switchboard. | Blood Bank will automatically thaw 4 units of FFP once blood group known. |
| **Gartnavel General Hospital** | | | |
| Phone numbers | Blood storage<br>(O Neg Blood | Key personnel | Coagulation factors |
| Call switchboard - 2222 and state "Major Haemorrhage", name of hospital and location. | GGH Theatre (3 units).<br>GGH Porter Fridge (4 units irradiated). | Blood Bank, Porters, Anaesthetist informed by switchboard. | Blood Bank will automatically thaw 4 units of FFP. |

Table continues on next page

Table continued from previous page

| Glasgow Royal Infirmary | | | |
|---|---|---|---|
| Phone numbers | Blood storage<br>(O Neg Blood) | Key personnel | Coagulation factors |
| Call Switchboard 2222 and state “Major Haemorrhage”, name of hospital and location.<br>Call Blood Bank 24666 / 25047. | Blood Bank - MacEwen Building.<br>A&E Fridge - Jubilee Building.<br>Satellite theatre fridge - Queen Elizabeth Building.<br>Labour Ward Fridge - Princess Royal Maternity. | Blood Bank, Porters, Anaesthetist informed by switchboard. | The first issue of FFP and platelets can be made without haematologist involvement. Subsequent requests must be authorised by the duty haematologist. |

# Management of Acute Kidney Injury (AKI)

## Introduction

The definition of AKI is abrupt and sustained decline in glomerular filtration rate leading to accumulation of urea and other chemicals. It is classed in to 3 stages (see table 1). Risk factors of developing AKI are listed in boxes 1 and 2.

### Table 1 – Stages of AKI

| AKI stage | Definition |
|---|---|
| I | Cr >150 - 200% from baseline ***or***<br>Acute increase of Cr >25 micromol/L/48 hours ***or***<br>UO < 0.5 ml/kg/hour for > 6 hours |
| II | Cr > 200 – 300% from baseline ***or***<br>UO < 0.5 ml/kg/hour > 12 hours |
| III | Cr > 300% from baseline ***or***<br>Cr > 350 micromol/L ***or***<br>UO < 0.3 ml/kg/hour for 24 hours or anuric for 12 hours ***or***<br>requires renal replacement therapy, irrespective of Cr |

**Note**: UO = urine output

**Box 1 – AKI risk factors**

**Clinical history**

- Kidney disease
- Heart failure
- Ischaemic heart disease
- Malignancy
- Liver disease
- Urological intervention

**During a hospital admission**

- Surgery
- IV contrast
- > 20 mmHg decrease in BP
- Urinary obstruction
- Hypovolaemia
- Malnourished

**Box 2 – AKI avoidable risk factors**

**Nephrotoxins**

- Angiotensin-converting enzyme inhibitors / Angiotensin-II receptor antagonists
- Non-steroidal anti-inflammatory drugs
- Antivirals / antifungals
- Vancomycin / Gentamicin
- Chemotherapy / contrast

**Contrast Administration**

If patient is at risk:

- Use low ionic low-osmolar contrast
- Fluids 1 ml/kg/hour fluid 6 - 12 hours pre- **and** post study

# Assessment / Monitoring

### AKI stage I

- Obtain clinical history. Check for risk factors (see box 1 on previous page), any pointers towards aetiology and review medication (see examples in box 2).
- Clinical examination:
  - Check patient's obs,
  - Fluid status (assess peripheral perfusion, JVP (central venous pressure, CVP), oedema, 3rd spacing) and urine output (UO).
- Investigations:
  - U&Es, urinalysis, MSSU, CXR, ECG.
  - **Consider** renal ultrasound (US), sepsis screen

### AKI stage II

As for Stage I but renal US within 24 hours and sepsis screen.

### AKI stage III

- As for stage II. Look for multi-organ failure and chase renal US report.
- Mandatory blood tests are: U&Es and $HCO_3^-$, CRP, creatine kinase, LFTs, $Ca^{2+}$, FBC, coagulation factors.
- **Consider**: amylase level, urine PCR if proteinuria, autoantibody screen if haematuria or proteinuria, microscopy if haematuria, myeloma screen, abdominal US.

**AKI complications** include: sepsis, acidosis, hyperkalaemia, multi-organ failure, oedema, respiratory failure, encephalopathy, serositis, haemorrhage.

# Management

### AKI stage I

- Stop nephrotoxins (see box 2 on previous page)
- Optimise fluid status.
  - Correct hypovolaemia, hydrate, optimise haemodynamics, keep accurate fluid balance chart.
  - Fluid challenge unless there is evidence of fluid overload.
    Aim for a mean arterial pressure > 65 or SBP > 100 mmHg.
  - **Consider**: vasoactive agents if hypotensive and not volume depleted.
  - Assess response and repeat U&Es. Aim for UO of 0.5 ml/kg/hour.
- Treat infection if present (see Infection Management Guidelines pages 211-254).
- Manage any contributing risk factors.
- **Consider**: inserting urinary catheter, seeking senior review, assessing CVP, reviewing medication and adjusting doses.
- Relieve obstruction if present with mandatory decompression, also request urgent urology review and/or discussion with interventional radiologist.

*Continues on next page*

*Management – AKI stage I continued*

- If evidence of rhabdomyolysis then:
  - Aim for UO > 100 ml/hour
  - Alternate Sodium chloride 0.9% IV with Sodium bicarbonate 1.26% IV
  - Keep urine pH > 6.5
  - Request surgical review if indicated

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**AKI stage II**

- Manage as per Stage I and also:
  - Seek senior review
  - Insert urine catheter and check urine volumes hourly.
- **Consider**:
  - CVP / cardiac monitoring, 12 hourly bloods and level 2 care.
  - Refer to the Renal team if likely to need renal replacement therapy or if no clinical improvement in 24 - 48 hours.

---

**AKI stage III**

- As per Stage II and also:
  - Refer to the Renal team and transfer to level 2 care.
  - Do cardiac monitoring
- **Consider**:
  - CVP line insertion and 12 hourly bloods
  - Refer to ITU if patient is in respiratory failure or there is multi-organ involvement.

## Referral Criteria to Renal Unit

- Urgent inpatient referral if:
  - High suspicion of rapidly progressive glomerulonephritis
  - Indication for dialysis (refractory increase $K^+$ > 6.5 mmol/L, or urea > 30 with (or without) Cr > 500 micromol/L, tumour lysis syndrome, refractory volume overload, refractory acidosis pH ≤ 7.1, complications of uraemia, severe poisoning, severe hypothermia).
  - Stage III AKI
  - Stage II AKI and unresponsive to treatment after 24 – 48 hours
  - Renal transplant patient
  - Dialysis patient prior to admission

Page oncall renal page 4603.

- Non-urgent inpatient referral if:
  - Stage II AKI
  - Nephrotic syndrome
  - Positive ANCA or ANA and proteinuria with or without haematuria
  - Malignant hypertension

Telephone renal secretary on 0141 211 2658 or fax 0141 211 2322, response within 1 working day.

Section 2

# Drug Overdose and Toxicity

# General Management of Overdoses and Toxicity

Most overdoses come to no harm. For all overdoses (even common ones) it is good practice to refer to TOXBASE www.toxbase.org (password required). Print out a copy of the advice to put in the patient's notes and follow the advice. If patient is unwell or you are not sure, discuss with a senior and contact the National Poisons Information Service (NPIS) on 0844 892 0111.

# Treatment of Paracetamol Overdose

This guideline has been updated to reflect the new guidance on management of oral paracetamol overdose issued from the Medicines and Healthcare Products Regulatory Agency (MHRA) in September 2012.

Further information can be found on www.toxbase.org (password required) (or contact the National Poisons Information Service (NPIS, 0844 892 0111)), including guidance for pregnant patients and management of IV paracetamol overdose and management of patients in whom IV treatment therapy is not appropriate.

## Introduction

In overdose the potential risk of a patient having significant liver damage is directly proportional to the amount of paracetamol ingested. The patient's risk of paracetamol-induced hepatotoxicity should no longer be stratified according to the presence of risk factors like glutathione deficiency or liver inducing enzymes. These factors are considered to be poorly evidenced. Instead patient management has been simplified to a single treatment line on the new paracetamol treatment nomogram. The other change is in the administration of acetycysteine IV in three sets of infusions with infusion 1 now given over 1 hour rather than 15 minutes.

## Management options

Acetylcysteine (N-acetylcysteine, Parvolex®, NAC) IV is still the treatment of choice. It can prevent paracetamol-induced hepatotoxicity if given during the first 8 hours of overdose. It may also be effective up to and possibly beyond 24 hours. Hypersensitivity and anaphylaxis reactions are not contraindications to using acetylcysteine (more guidance on page 40).

Follow the initial management options outlined in the following pages with further guidance on www.toxbase.org (password required). When checking paracetamol plasma level also check patient's U&Es, Cr, bicarbonate, LFTs, INR and FBC.

### < 8 hours after oral paracetamol ingestion

- Consider activated charcoal administration if > 150 mg/kg paracetamol has been taken within a 1 hour period.
- For obese patients (> 110 kg) the toxic dose in mg/kg should be calculated using 110 kg, rather than their actual weight.
- ***Wait until 4 hours from ingestion then measure plasma level and send for urgent analysis.*** Await result before deciding whether treatment is required (provided result can be obtained and acted upon within 8 hours of ingestion). Paracetamol plasma levels < 4 hours after ingestion cannot be interpreted.
- If biochemical results suggest acute liver injury then double-check history of paracetamol ingestion, especially the timing. Consider treatment with acetylcysteine infusion – page 40.
- Once paracetamol plasma level is known then use the revised treatment nomogram (page 39) to assess the risk of severe liver damage. If the paracetamol level is above the treatment line then treat with acetylcysteine infusion – see dosing table page 40.

*Continues on next page*

## 8 - 24 hours after ingestion

- Send for urgent paracetamol plasma level. If the dose ingested is suspected to be > 150 mg/kg within 1 hour ***do not wait for result - commence treatment with acetylcysteine (dosing table page 40) immediately***. The efficacy of acetylcysteine rapidly declines during this period so do not delay treatment.
- For obese patients (> 110 kg) the toxic dose in mg/kg should be calculated using 110 kg, rather than patient's actual weight.
- Monitor blood results (details on previous page) and if results suggest acute liver injury then double check history of paracetamol ingestion, especially the timing. Consider treatment with acetylcysteine infusion – page 40.
- Acetylcysteine can be discontinued if plasma paracetamol concentration is later reported to be below the treatment line on the graph on page 39, provided the patients is asymptomatic and LFTs, serum creatinine and INR are normal.

## > 24 hours after ingestion

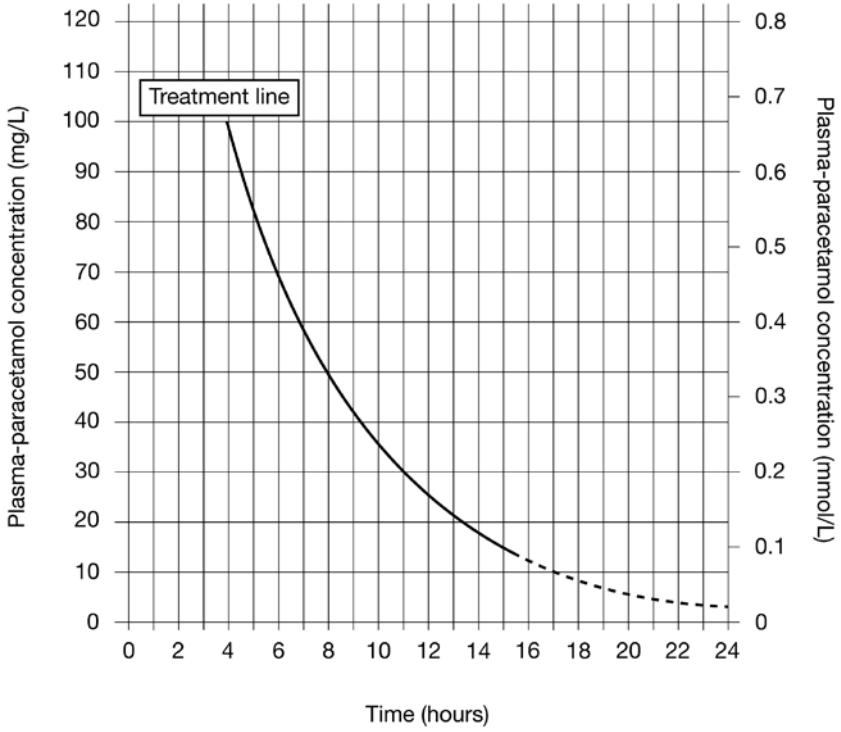
- A plasma concentration measured at this time is likely to be below the limit of detection, even after a substantial overdose. Treat with acetylcysteine if > 24 hours after a suspected paracetamol ingestion the:
  - measured concentration $\geq$ 5mg/L at $\geq$ 24 hours ingestion (indicative of a very large overdose) or
  - INR is normal (is $\leq$ 1.3) but ALT > 2 times the upper limit of normal or
  - INR is > 1.3 (in the absence of any obvious cause) but ALT is normal (< 2 times the upper limit of normal) or
  - the patient has jaundice or hepatic tenderness
- For obese patients (> 110 kg) the toxic dose in mg/kg should be calculated using 110 kg, rather than patient's actual weight.
- Monitor blood tests (details on previous page) as well as venous or arterial blood gases. If INR or LFTs deranged then repeat bloods at 8 – 16 hours and consider other causes. Stop acetylcysteine if INR is $\leq$ 1.3 and ALT has not increased further, otherwise continue and recheck bloods at 8 – 16 hour intervals.
- For further management guidance refer to TOXBASE www.toxbase.org (password required) or contact National Poisons Information Service (NPIS, 0844 892 0111).

## Staggered overdoses

- Defined as paracetamol taken over $\geq$ 1 hour.
- Send for paracetamol levels and monitor blood tests (details on previous page). **Note:** In staggered overdose the treatment nomogram is unreliable.
- Clinically significant toxicity is unlikely if, following at least 24 hours since the last paracetamol ingestion, the following criteria is met:
  - paracetamol measured concentration is not detectable (< 5 mg/L)
  - INR $\leq$ 1.3
  - plasma creatinine normal
  - ALT < 2 times the upper limit of normal
  - patient asymptomatic

*Continues on next page*

- If there is any uncertainty, then treat with acetylcysteine (dosing table on the next page). For further management guidance refer to TOXBASE www.toxbase.org (password required) or contact National Poisons Information Service (NPIS, 0844 892 0111).




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## Paracetamol overdose treatment nomogram

- Determine the need for acetylcysteine by plotting the measured plasma paracetamol level (in mg/L) against the time since ingestion. If plasma level falls above the line then give acetylcysteine as detailed on the next page.
- If timing of ingestion is unreliable then treat with acetylcysteine regardless of whether the plasma level is above or below the treatment line.
- If overdose is staggered (taken over longer than 1 hour) then the nomogram is unreliable; see previous page.

**N.B.** In NHSGGC paracetamol plasma levels reported in units of mg/L.

*Continues on next page*

**Table 1 – Acetylcysteine adult dosing table**

Each ampoule = 200 mg/ml acetylcysteine

| Regimen | 1st infusion | | 2nd infusion | | 3rd infusion | |
|---|---|---|---|---|---|---|
| **Infusion fluid** | 200 ml 5% glucose or sodium chloride 0.9% | | 500 ml 5% glucose or sodium chloride 0.9% | | 1000 ml 5% glucose or sodium chloride 0.9% | |
| **Preparation** | Use a 250 ml infusion bag and remove 50 ml prior to adding in the required drug volume | | Add the required volume of the drug to the 500 ml infusion bag | | Add the required volume of the drug to the 1000 ml infusion bag | |
| **Duration of infusion** | 1 hour | | 4 hours | | 16 hours | |
| **Drug dose** | 150 mg/kg acetylcysteine | | 50 mg/kg acetylcysteine | | 100 mg/kg acetylcysteine | |
| **Patient weight[1] (kg)** | **Ampoule volume[2] (ml)** | **Infusion rate (ml/hour)** | **Ampoule volume[2] (ml)** | **Infusion rate (ml/hour)** | **Ampoule volume[2] (ml)** | **Infusion rate (ml/hour)** |
| **40 - 49** | 34 | 234 | 12 | 128 | 23 | 64 |
| **50 - 59** | 42 | 242 | 14 | 129 | 28 | 64 |
| **60 - 69** | 49 | 249 | 17 | 129 | 33 | 65 |
| **70 - 79** | 57 | 257 | 19 | 130 | 38 | 65 |
| **80 - 89** | 64 | 264 | 22 | 131 | 43 | 65 |
| **90 - 99** | 72 | 272 | 24 | 131 | 48 | 66 |
| **100 - 109** | 79 | 279 | 27 | 132 | 53 | 66 |
| **≥ 110** | 83 | 283 | 28 | 132 | 55 | 66 |

[1] Dose calculations are based on the weight in the middle of each band.

[2] Ampoule volume has been rounded up to the nearest whole number.

## Important notes

1. **Obese patients (> 110 kg**) – the dose should be calculated using a weight of 110 kg rather than the patient's actual weight.
2. **Patients < 40 kg** – access paediatric dosing table through TOXBASE www.toxbase.org (password required).
3. Hypersensitivity and anaphylaxis reactions with acetylcysteine are **not contraindications** as the benefit of treatment still outweighs the risk of not. True anaphylaxis is rare with acetylcysteine but can be managed by stopping the infusion, managing the reaction as per page 18 and then re-starting at a slower rate (e.g. give infusion 1 over 2 hours and infusion 2 over 8 hours).
4. Re-check INR, Cr, bicarbonate, LFT at or just before the end of the 21 hour acetylcysteine infusion and manage as per guidance in TOXBASE.

# Reversal of Opioid-induced Respiratory Depression

This guideline relates to the reversal of accidental opioid-induced respiratory depression, rather than intentional overdose. For management of narcotic overdose, contact the National Poisons Information Service (telephone 0844 892 0011) or consult TOXBASE – www.toxbase.org (password required).

## Management

Reduced conscious level is usually used to predict patients at risk of severe respiratory depression. If the patient is unrousable:

1. Give oxygen therapy (see pages 128 and 131).
2. Give naloxone. Balance the risk of withholding naloxone against a possible transient worsening of pain if given. If necessary, contact a senior colleague for advice.

   **Naloxone IV bolus:**

   **Naloxone IV 100 - 200 micrograms, then increments of 100 micrograms every 2 minutes as required according to response.**

   Observe patient carefully for recurrence of CNS and respiratory depression. The plasma half-life of naloxone is shorter than that of all opioid analgesics – *therefore repeated doses of naloxone may be required.*

   **Naloxone IV infusion:**

   **N.B.** Administration guidance from TOXBASE

   Naloxone infusion may be useful where repeated doses are required. An infusion of 60% of the total dose infused over 1 hour is a useful starting point.

   **Dilution:** Make up a solution of naloxone 10 mg/50 ml as follows:

   - Draw up 10 mg of naloxone from 25 ampoules, each containing 400 micrograms/ml (total volume: 25 ml).
   - Dilute the 10 mg concentrate with 25 ml of glucose 5% to give a final volume 50 ml and a concentration of 200 micrograms/ml.
   - Infuse solution using an IV pump, adjust dose to clinical response. Infusions are not a substitute for frequent review of the patient's clinical state.

   **Dose example**: If the total repeated doses required to maintain patient with satisfactory ventilation for at least 15 minutes add up to 4 mg then the infusion rate would be 60% of this dose which is 2.4 mg (12 ml) / hour.
3. Observe patients for at least 6 hours after the last dose of naloxone. Monitor BP, pulse, respiratory rate, oxygen saturation and conscious level at least every 15 minutes initially.
4. If no response to naloxone, do not delay establishing a clear airway, adequate ventilation and oxygenation
5. If pulmonary oedema is a complication, then assisted ventilation with positive end-expiratory pressure may be necessary.

# Lithium toxicity

Normal range 0.4 - 1 mmol/L. Plasma lithium level > 1.5 mmol/L may be fatal and requires urgent medical treatment. In overdose, there may be a delay of symptoms (> 12 hours).

## Common features

- Early features of toxicity are non-specific e.g. apathy, restlessness and can be followed by: confusion, vomiting, diarrhoea, loss of appetite, slurred speech, abnormal drowsiness or sluggishness, severe tremor or twitching, muscle weakness, blurred vision, ringing in ears, dizziness, loss of balance, clumsiness.
- Severe toxicity: convulsions, coma, renal failure, hypotension, dehydration, electrolyte imbalances and death.

## Common causes of toxicity

- Dehydration, renal dysfunction, infection, interacting medication e.g. diuretics, non-steroidal anti-inflammatories (see BNF for more details).

## Management of toxicity

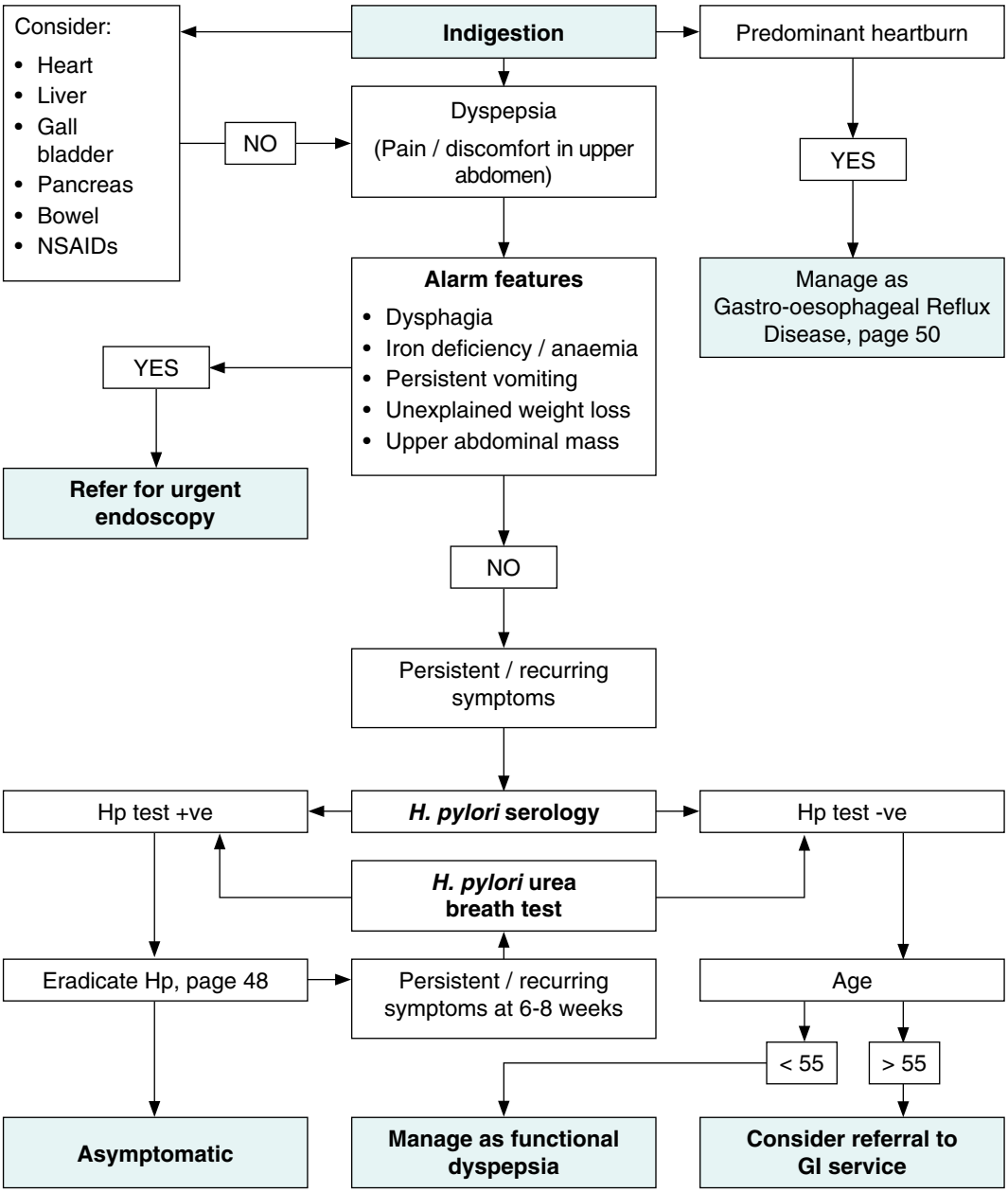
- If there are concerns that the patient could be lithium toxic, then seek advice from senior medical staff, withhold lithium and obtain lithium level. Check urea and electrolytes and thyroid function tests. Closely monitor fluid balance.

See Appendix 3 for information on therapeutic monitoring of lithium.

Section 3

# Gastrointestinal System

# Management of Dyspepsia



# Management of Constipation

## Introduction

This guideline applies to patients who are initiated on laxatives during their hospital stay or to patients who are not responding to their current laxative therapy.

**N.B**.: *Laxatives are **contraindicated** in patients with intestinal obstruction. If suspected refer to specialist surgical team*.

### Assessment / monitoring

Identify possible causes:

- Underlying disease e.g. hypothyroidism, hypercalcaemia.
- Mechanical obstruction e.g. rectal tumour.
- Immobility / dehydration e.g. stroke / diabetes mellitus.
- Drugs e.g.
  - Opiates (including co-codamol and dihydrocodeine);
  - Anticholinergics (tricyclic antidepressants, oxybutynin);
  - Verapamil;
  - Aluminium containing antacids;
  - Iron and calcium containing preparations.

#### Check

- Serum U&Es
- Creatinine
- Calcium
- Thyroxine (T4)
- Glucose

## General management

**Rectal examination:**

- Hard faeces – (prescribe a faecal softener e.g. lactulose – see table on following pages).
- Soft faeces – (prescribe a stimulant laxative e.g. senna – see table on following pages).
- Impaction – (for enema e.g. sodium citrate micro-enema or phosphate enema – see table on following pages).
- Empty rectum – (suspect obstruction and obtain plain abdominal x-ray).

## Educate patient

- Increase dietary fibre (bran, fruit, vegetables).
- Increase mobility.
- Ensure adequate fluid intake (especially if on bulk forming laxative e.g. ispaghula husk, or high fibre diet).

# Drug therapy / treatment options

| **Acute constipation.** (Constipation of recent onset due to a period of illness or immobility, drug therapy, changes in diet or fluid intake. Laxatives should only be given for short-term use.) | | |
|---|---|---|
| **Laxative** | **Dose** | **Notes** |
| Senna tabs | 2 - 4 tablets at night | Liquid preparation also available: 10 ml senna liquid = 2 senna tablets. |
| *Or* | | |
| Glycerol suppositories | 4 g PR daily | Moisten suppositories with water for ease of insertion. |

| **Chronic constipation** (Requires long-term management.) | | |
|---|---|---|
| **Laxative** | **Dose** | **Notes** |
| Ispaghula husk (Fybogel®) | 1 sachet twice daily | Ensure adequate fluid intake. If ineffective after several days add senna 2 - 4 tablets at night (short-term only). |
| *Or* | | |
| Lactulose | 15 ml twice daily regularly | If above option is not effective / appropriate. |
| +/- senna | 2 tablets at night | |
| *Or* | | |
| Macrogol Oral Powder (Laxido Orange®) | 1 - 3 sachets daily | If above options are not effective/ appropriate.<br>Ensure adequate fluid intake. |
| +/- senna tabs | 2 tablets at night | |

| **Opioid-induced constipation** | | |
|---|---|---|
| **Laxative** | **Dose** | **Notes** |
| Senna tabs | 2 - 4 tablets at night | |
| *and either* | | |
| Lactulose | 15 ml twice daily regularly | |
| *Or* | | |
| Sodium Docusate | 100 - 500 mg daily | |
| *Or* | | |
| Co-danthramer capsules | 1 - 2 at night | **For terminally ill patients only.** |
| Co-danthramer liquid | 5 - 10 ml at night | Titrate dose upwards as necessary. |

Table continues on next page

| Table continued from previous page | | |
|---|---|---|
| **Rectal impaction*** | | |
| **Laxative** | **Dose** | **Notes** |
| Bisacodyl suppository AND Glycerol suppository | 1 of each | |
| Sodium citrate microenema | 1 at night | |
| *If no result, followed by:* | | |
| Phosphate enema | 1 in the morning | Do not use more than twice a day. |
| Arachis oil retention enema | 1 | Avoid if nut allergy. |
| *If no result, followed 6 - 8 hours later by either:* | | |
| Sodium citrate microenema | 1 | |
| *Or* | | |
| Phosphate enema | 1 | |
| Macrogol Oral Powder (Laxido Orange®) | 8 sachets daily for up to 3 days** | For use in resistant cases of impaction.<br>Ensure adequate fluid intake. |

* In some cases of rectal impaction, manual evacuation may be required. Seek advice from senior medical staff.

** May not be possible to use this dose in the frail elderly.

***Note:*** *Patients unable to swallow, but with a nasogastric or RIG/PEG tube in situ can have certain laxative preparations administered via the tube. Contact clinical pharmacists for details.*

## Management of Diarrhoea

| | |
|---|---|
| Oral rehydration salts e.g. Dioralyte® | 1 - 2 sachets after every loose motion. Each sachet is reconstituted with 200 ml of water. |
| Loperamide | 4 mg initially followed by 2 mg after each loose stool, up to a maximum of 16 mg daily. |

**Note**: *If Clostridium difficile is suspected, see Infections section. In such cases loperamide is* ***not appropriate.***

# Management of *Helicobacter pylori*

*Helicobacter pylori* (*H. pylori*) is a bacterium colonising the gastric mucosa and may be the causative agent in a number of gastrointestinal pathologies.

## Eradication - which patients?

- All patients with proven duodenal ulcers.
- Patients with gastric ulcer.
- Patients with *H. pylori* and a strong family history of gastric cancer.
- Patients with epigastric pain in the absence of an ulcer.

## Assessment / monitoring

Initial testing for *H. pylori* may be done by laboratory-based serology, urea breath test and stool antigen test. Re-testing should always be done using urea breath test.

## Drug therapy

One week therapy with a proton pump inhibitor (PPI) and two antibiotics is recommended:

**First line –**

**Omeprazole oral 20 mg twice daily *(or* lansoprazole oral 30 mg twice daily)**

**and**

**Clarithromycin oral 500 mg twice daily**

**and**

**Amoxicillin* oral 1 g twice daily.**

***In penicillin allergy use tetracycline oral 500 mg twice daily.***

**Second line –**

Substitute:

**Clarithromycin for metronidazole oral 400 mg twice daily.**

- Patients should be counselled on the importance of compliance before starting treatment and in those patients taking metronidazole on the avoidance of alcohol because of the risk of a disulfiram-like reaction.
- After 1 week's treatment all medication can be stopped, except where ulcers have bled or perforated, when a PPI will be continued.
- A breath test should be carried out 28 days after completion of treatment to check that eradication has been successful if the patient is still symptomatic.

**N.B.** Healing of gastric ulcers must be confirmed by endoscopy after 6 - 8 weeks.

# Management of Gastroduodenal Ulcers

## Introduction

If *H.pylori* infection demonstrated, treat with eradication therapy, as outlined on previous page.

## Drug therapy

### Proton pump inhibitors

**Omeprazole oral 40 mg once daily for 4 - 8 weeks or**

**Lansoprazole oral 30 mg once daily for 4 - 8 weeks**

*If the ulcer is associated with NSAID:*

- Discontinue the NSAID.
- Repeat endoscopy 2 - 4 weeks after completion of therapy to confirm healing and to check for *H.pylori*. If latter is positive, eradicate infection.
- If the NSAID needs to be continued or restarted, use in combination with a PPI e.g. :

  **omeprazole oral 20 mg once daily or**

  **lansoprazole oral 30 mg once daily**

  irrespective of *H. pylori* status.

### IV proton pump inhibitors

- If the patient is unable to take oral therapy give:

  **omeprazole 40 mg by slow IV bolus injection**

- If patient has had endoscopic haemostasis for a bleeding ulcer give:

  **omeprazole infusion, initial 80 mg dose** (give 80 mg in 100 ml sodium chloride 0.9% infused over 40 - 60 mins)

  ***followed by:***

  **continuous infusion of 8 mg/hour for 72 hours** (make up 80 mg in 100 ml sodium chloride 0.9%, infuse at 10 ml (8 mg) per hour over 10 hours for a total of 72 hours, a total of 8 infusion bags have to be prepared.)

  ***followed by maintenance dose:***

  **omeprazole oral 20 mg each day for 8 weeks**

**N.B.** Continuous infusion of omeprazole is an unlicensed use. Bags should only be prepared immediately before use as no stability data beyond this time period.

# Management of Gastro-oesophageal Reflux Disease (GORD)

## General management

- Lifestyle changes will include:
  - weight reduction
  - reduce alcohol
  - stop smoking
  - avoid stooping
  - raise head of bed
  - avoid foods that lower LOS (lower oesophageal sphincter) pressure (e.g. caffeine, chocolate, and onions).
- Review concurrent drug therapy:
  - Avoid NSAID (non-steroidal anti-inflammatory drugs) and consider alternatives if possible for drugs likely to lower LOS pressure (e.g. any drugs with anticholinergic side effects, SSRIs, calcium-channel blockers)

## Treatment options

### Mild symptoms

**Co-magaldrox (Mucogel®) oral 10 - 20 ml after meals and at bedtime, or when required**

**or**

**Peptac® oral 10 - 20 ml after meals and at night.**

**N.B.** Avoid in cardiac failure, renal disease and hepatic disease.

### Persisting symptoms

**Omeprazole oral treatment dose 40 mg once daily for 4 - 8 weeks, then maintenance dose 20 mg once daily or**

**Lansoprazole oral treatment dose 30 mg once daily for 4 - 8 weeks, then maintenance dose 15 mg once daily.**

### Long-term maintenance

- Aim for lowest dose proton pump inhibitor (PPI) needed to control symptoms.
- Encourage 'on demand' PPI treatment especially for endoscopy-negative reflux disease.

#### Ongoing symptoms

- Try higher dose PPI and seek specialist advice.

# Management of Upper Gastrointestinal (GI) Haemorrhage

## Introduction

- 80% of upper GI bleeding will stop spontaneously.
- Age, co-morbidity and signs of significant blood loss (e.g. shock and melaena) increase risk.
- Liver disease and variceal bleeding have much higher mortality rates (see separate guidelines on pages 56, 60 and 62).

## Assessment

- Assess pulse and BP (including postural blood pressure if not hypotensive).
- Check for evidence of significant blood loss (including rectal examination for melaena - if melaena is present it implies that there has been significant blood loss).
- Check FBC, U&Es and LFTs.
- Check coagulation if suspected liver disease or on anticoagulation.
- Assess co-morbidity.
- Check medication – NSAIDs (non-steroidal anti-inflammatory drugs), aspirin, anticoagulants.
- Scoring systems can be used to assess risk in these patients and local protocols for individual hospitals exist, dependent on resources and endoscopy services. The Rockall score is the most commonly used endoscopy-based risk score and the Glasgow Batchford Score (GBS) is the best early (pre-endoscopic) risk score. However, if a patient is haemodynamically unstable with ongoing bleeding, they should be discussed with the on-call surgical team / endoscopist. Other patients should be endoscoped on the next available list.
- Out-patient management – If the patient's parameters and clinical status fulfil **all** criteria of table 1 (GBS = 0), then patient can be discharged and managed in out-patient setting (see Table 1 below).

**Table 1 – Criteria for out-patient management (GBS = 0)**

| Parameter | Value |
|---|---|
| Urea | < 6.5 mmol/L |
| Hb | > 130 g/L (men)<br>> 120 g/L (women) |
| Systolic BP | ≥ 110 mmHg |
| Pulse | <100 bpm |
| **Clinical Status** | |
| Absence of melaena, syncope, cardiac failure or hepatic disease | |

GBS - The Lancet, 356 (Iss 9238), Blatchford O, Murray WR, Blatchford M. Risk score for treatment of upper-gastrointestinal haemorrhage, page 1318-21. Copyright (2013), adapted with permission from Elsevier.

*Continues on next page*

## General management

All patients:

- Group and save or cross-match as clinically indicated
- Stop NSAIDs, aspirin and anticoagulants
- Consider reversing anticoagulation (depends on severity of bleeding and indication for anticoagulation, see page 85)
- Repeat Hb as clinically indicated

Patients with haemodynamic compromise and/or significant comorbidities have higher mortality, particularly if elderly. In these patients:

- Crossmatch 4 units
- IV access x 2 - use green (18G) needle or larger
- Consider HDU
- Resuscitate aggressively. Use blood volume expanders or sodium chloride 0.9% to keep pulse < 100 bpm, systolic BP > 100 mmHg, urine output > 30 ml/hour and transfuse as clinically indicated.
- If resuscitation difficult consider CVP monitoring.

Contact senior support to decide on timing of urgent endoscopy.

## Endoscopy

- Fast for 3 hours
- Consent
- Venflon in situ
- Ensure case notes and observation charts go with patient.

## Post endoscopy

**If no abnormality found and no drop in haemoglobin:**

There is a low risk of re-bleeding. Consider patient for early discharge.

**If peptic ulcer disease is found:**

a. Stop NSAIDs , aspirin, clopidogrel or anticoagulants in an acute bleeding situation and reassess the risk versus benefit of reintroduction once the bleeding is controlled. For NSAIDs and antiplatelets use low dose monotherapy if possible and if required concomitant proton pump inhibitor (PPI):

**Lansoprazole oral 30 mg each day or Omeprazole oral 20 mg each day**

If patient is on dual antiplatelet therapy for coronary stents, discuss the risks with the interventional cardiologist. Continuing with a single antiplatelet agent with PPI may be appropriate until repeat endoscopy.

*Continues on next page*

*Post endoscopy continued*

b. Arrange $C^{13}$ Urea Breath Test:
   - If positive for *H. pylori* – see eradication regimen page 48.
   - If negative for *H. pylori* and not on NSAIDs – maintain on lifelong PPI (see above for choice and dose).
   - If re-bleeding occurs (fresh melaena or haematemesis associated with a drop in Hb of 20 g/L) - seek senior help, including surgical review.
   - If varices, refer to separate guideline, page 60.
   - Give specific treatment for other pathologies as indicated.
   - Discuss with gastroenterologist as required.

c. If stigmata for high risk of re-bleeding (e.g. active bleeding at endoscopy or visible vessel) then the endoscopist may recommend:

   **Omeprazole IV infusion (Hong Kong Protocol) – page 49 for dose and administration details.** This is an unlicensed use and so should only be prescribed at the request of a consultant.

   These patients should remain in hospital for 96 hours to monitor for re-bleeding. After infusion initiate PPI oral therapy (see previous page for choice and dose).

## On discharge

- Arrange $^{13}C$ Urea Breath Test in 8 weeks if *H. pylori* eradication therapy given.
- Continue PPI for 6 weeks and then change to $H_2$ antagonist prior to breath test.
- Repeat OGD (Oesophagogastroduodenoscopy) in 8 weeks if gastric ulcer found.

# Management of Severe Exacerbation of Inflammatory Bowel Disease

## Assessment / monitoring

**On admission**

- Stool culture and *Clostridium difficile* toxin.
- Stool chart (kept by nursing staff).
- BP / pulse / temperature – frequency depends on initial findings.
- Bloods – FBC; CRP or ESR; U&Es; LFTs; blood cultures.
- X-ray – plain film of abdomen.
- If features suggesting severe disease present, seek immediate senior review.
- Unprepared sigmoidoscopy in new patient.

## General management and treatment options

- Avoid anti-diarrhoeal agents
- Give **IV fluids**
- Give **hydrocortisone sodium succinate IV infusion 100 mg every 6 hours or methylprednisolone 30 mg IV infusion every 12 hours.** Check which drug is used on your site before prescribing.
- Give low residue diet / oral fluids
- Give high calorie supplements
- If Hb < 90 g/L – transfuse
- High risk of venous thromboembolism – give thromboprophylaxis (unless contraindicated):

  **enoxaparin SC 40 mg once daily (20 mg once daily if eGFR < 30 ml/minute /1.73m$^2$ as these patients are at risk of DVT.**
- Involve gastroenterologist / gastrointestinal surgeon.

**Note:** Caution with:

- Narcotics
- Antispasmodics

Patient with abdominal pain must be seen and assessed before prescribing analgesia.

- Hypokalaemia
- Barium enema

Discuss with radiologist / gastroenterologist.

**Continues on next page**

**General management and treatment options continued**

## Ongoing management

- Monitor Hb, WCC, U&Es, CRP daily
- Daily abdominal film whilst on IV steroid therapy and arrange surgical review if transverse or ascending colon diameter > 6 cm.
- Light diet
- A CRP > 45 or the stool frequency > 8 at day 3 are bad prognostic signs and senior review and/or surgical review should be undertaken immediately.

## Drug treatment after 5 - 7 days

- Change IV hydrocortisone to:

  **prednisolone oral 40 mg each day. Reduce no faster than by 5 mg every 5 - 7 days. Normally there is gradual reduction over a 4 - 8 week period if CRP and stool frequency falling.**

- **Add mesalazine oral (Pentasa® Granules MR 2 - 4 g per day in 2 divided doses or Asacol® MR 2.4 - 4.8 g daily in 2 divided doses or Mezavant® XL 2.4 g once daily preparation).**
- Rectal preparations may be useful in proctitis, left sided disease and Crohn's disease of the rectum and anus. Seek specialist advice.

# Discharge

Normally discharged when:

- Non-toxic
- Stool frequency decreased, consistency increased and macroscopic blood decreased
- Lab parameters stable
- Follow-up OPD appointment made

# Management of Decompensated Liver Disease



## Assessment / monitoring

- Bloods for FBC, coagulation screen, U&Es, LFTs, glucose
- Signs of chronic liver disease
- Arrange ultrasound scan of abdomen
- Assess for alcohol withdrawal
- Dietary assessment
- Liver screen including AFP (alpha fetoprotein) if not previously performed
- **In encephalopathy** (signs = mental slowness, confusion, drowsiness, liver flap):

  Assess for the following precipitants and treat as appropriate:

  - Sepsis
  - Culture blood and urine
  - Tap ascites if present for WCC count, protein content and culture (see below)
  - Arrange chest x-ray
  - Bleeding
  - Renal failure, electrolyte abnormalities
  - Constipation
  - Medication (e.g. sedatives or over-diuresis)
- **In renal impairment:**
  - Assess for potentially reversible factors – dehydration, diuretics, sepsis, intrinsic renal disease.
  - Renal tract US to exclude obstruction. Urine dipstick – if hepatorenal should be nothing abnormal detected. If blood and protein consider renal causes.
  - Assess for hydration.
- **If ascites is present:**
  - Consider other causes of ascites (e.g. malignancy, Budd-Chiari syndrome or cardiac failure).
  - Perform diagnostic ascitic tap. Aspirate 50 ml of fluid (normally straw coloured) and send for:
    - Microbiology – WCC and culture in blood culture bottle (anaerobic and aerobic)
    - Biochemistry – total protein and albumin
    - Cytology - send if malignancy suspected or SAAG (serum-ascites albumin gradient) < 11. Obtain > 100 ml of fluid to increase yield.

*Continues on next page*

- SAAG can differentiate ascites resulting from portal hypertension and from other causes. It is more useful than the protein based exudate / transudate concept. Calculate SAAG by:

  SAAG = (serum albumin) – (ascites albumin)

  Obtain both values on the same day. If SAAG > 11 g/L then ascites very likely the result of portal hypertension (97% accuracy).

- Table 1 lists the major differential diagnoses based on the SAAG.

**Table 1 – Differential diagnoses of ascites based on serum-ascites albumin gradient**

| **SAAG ≥ 11 g/L** | **SAAG < 11 g/L** |
|---|---|
| Cirrhosis | Diffuse peritoneal metastases |
| Alcoholic hepatitis | Tuberculous peritonitis |
| Cardiac ascites | Pancreatic ascites |
| Massive liver metastases | Nephrotic syndrome |

# General management and drug therapy

## Diet

- Aim for high protein, high calorie diet.
- Reduce protein slowly if encephalopathic.
- Restrict dietary salt if ascites is present.
- Give:

  **Vitamin K (phytomenadione) 10 mg slow IV injection over 3 - 5 minutes.**

  **Note**: *This will not correct clotting unless there is a deficiency (can occur in obstructive liver disease or prolonged malnutrition) but will ensure patient's level is replete.*

- Consider **DVT prophylaxis** (see page 66).
- **If history of alcohol abuse is suspected:**

  **Pabrinex® (contains thiamine)** – see vitamin prophylaxis flowchart page 176.

**Continues on next page**

**General management and drug therapy continued**

## Management of encephalopathy

- Assess for precipitating factors (see under 'Assessment and monitoring' section) and treat as appropriate. If sepsis suspected, treat with antibiotics. Remember typical signs of sepsis may be masked. Use broad-spectrum antibiotics (see page 211).
- Stop sedatives
- Give **lactulose oral 20 ml three times daily (titrate dose to give three soft motions per day).**

## Management of ascites

- If ascitic WCC > 500 /mm$^3$ or neutrophil count > 250 /mm$^3$, treat as for spontaneous bacterial peritonitis (SBP) (see below).
- Low salt diet
- Diuretics – initially use:

  **Spironolactone oral 100 - 400 mg each day**

  Seek senior advice if renal impairment or high potassium. Titrate dose / consider adding furosemide according to weight and renal function. Aim for weight reduction of no more than 1 kg per day.
- If ascites is causing respiratory compromise or is not responding to above measures consider large volume paracentesis.
- Treat Spontaneous Bacterial Peritonitis (SBP) once diagnosis confirmed with:

  **Suitable antimicrobial (see Infections section page 238)**

  **Salt poor albumin (100 ml of 20 %) IV infusion 1.5 g/kg on day one then 1 g/kg on day 3**
- Prophylaxis of SBP in:
  - patients with one episode proven SBP, either previously or currently (once current episode treated)
  - patients with total ascitic protein < 10 g/L

  Prescribe: **norfloxacin oral 400 mg once daily for prophylaxis.**

**Continues on next page**

**General management and drug therapy continued**

## Management of renal impairment

- Catheterise (strict input / output chart)
- Stop diuretics
- Assess hydration status. If clinically dehydrated:

  **Sodium chloride 0.9% IV infusion (1 - 1.5 litres is reasonable)**

  If evidence of ascites and peripheral oedema:

  **Salt poor albumin 20% IV, 2 x 100 ml each day** and consider:

  **Terlipressin IV – initially 0.5 mg 6 hourly. Titrate dose over 72 hours in discussion with the local gastroenterology team.**

  Terlipressin is contraindicated in ischaemic heart disease / peripheral vascular disease and arrhythmias.

If no improvement in urine output after above measures seek senior review and consider central venous pressure monitoring.

Jaundiced patients who suffer from alcoholic liver disease should be discussed with the local gastroenterology team regarding eligibility for inclusion in the STOPAH (Steroids or Pentoxifylline for Alcoholic Hepatitis) trial.

# Aminoglycoside in decompensated liver disease

Gentamicin should be avoided in patients with decompensated liver disease (jaundice, ascites, encephalopathy, variceal bleeding or hepatorenal syndrome). See infection management section or contact microbiology / infections diseases unit for advice.

# Other information

## For further monitoring

- Daily FBC, U&Es until improving
- Coagulation screen and LFTs 2 - 3 times per week
- Daily weight
- Monitor daily for encephalopathy

## Pre-discharge

- Aim to stabilise weight, mental state and diuretics dose prior to discharge
- Counsel about alcohol. Liaise with alcohol support services
- Arrange clinic review

# Management of Suspected Variceal Bleeding

## Assessment

- Check pulse and BP (including postural drop if not hypotensive).
- Assess for stigmata of chronic liver disease.
- Check FBC, coagulation, U&Es and LFTs.
- Cross-match 6 units of blood.

## Management

The following management plan should be instituted in all patients with suspected variceal haemorrhage on the basis of having evidence of chronic liver disease and evidence of a significant gastrointestinal bleed **prior to** the diagnosis of variceal bleed being confirmed.

- If patient is shocked (pulse > 100 bpm, systolic BP < 100 mmHg and evidence of bleeding) should have a urinary catheter inserted and consideration of CVP line insertion.
- Consider admission to HDU.
- Correct any clotting and platelet abnormality (discuss with haematology).
- Resuscitate with blood or colloid aiming to maintain Hb > 80 g/L, pulse < 100 bpm, systolic BP > 90 - 100 mmHg, CVP of 8 - 10 cm and urine output greater than 30 ml/hour. Resuscitation and transfusion requirements also depend on patient's age and co-morbidities.
- Start appropriate drug therapy (see 'Drug therapy' section of this guideline).
- If ascites is present perform an ascitic tap.
- Seek help from seniors:
  - If stable should be listed for urgent endoscopy.
  - If unstable, liaise with on-call endoscopist. A Sengstaken tube should only be inserted in exceptional circumstances by an experienced member of staff. Anaesthetic support to protect the airway followed by transfer to ITU may be necessary.

*Continues on next page*

## Drug therapy

- Unless contraindication (cardiovascular disease) start:

  **Terlipressin 2 mg by IV bolus followed by 1 - 2 mg every 4 to 6 hours until bleeding is controlled, for up to 48 hours.**

  **Octreotide** can be used if terlipressin contraindicated, but this use is unlicensed and therefore should be discussed with seniors first.

- Start antibiotics – use broad spectrum antibiotic cover:

  **Co-amoxiclav IV 1.2 g every 8 hours (or clarithromycin IV 500 mg every 12 hours if penicillin allergy).** If antibiotic therapy not otherwise required, continue for 7 days (when appropriate observe IV to oral switch).

## Management once stable

- Enter into a variceal eradication programme – discuss with gastroenterologist.
- Start **propranolol oral 40 mg twice daily if no contraindication and titrate up to 160 mg once daily sustained release preparation if tolerated.**
- Give advice on alcohol intake if appropriate – abstinence alone can reduce the portal pressure.

# Management of Acute Liver Failure

**Definition of Acute Liver Failure**: Encephalopathy developing in a person with acute hepatic dysfunction within 8 weeks of the onset of jaundice.

## Introduction

- Most acute admissions for liver failure occur in patients with pre-existing liver disease.
- Acute liver failure strictly refers to those patients without such a history, and is much rarer.
- The guidelines, Acute Liver Failure and Management of Decompensated Liver Disease, are intended to help with both the acute case and with the deterioration of chronic cases.



### Aetiology

The causes of acute liver failure in the UK are, in order of incidence:

- Paracetamol overdose (70%)
- Viral Hepatitis (8.4%)
- Idiosyncratic drug reaction (5.1%)
- Budd-Chiari (2.1%)
- Autoimmune (2%)
- Ischaemic (2%)
- Miscellaneous (10.4%)

(Reference: Edinburgh Royal Infirmary 2009)

### Clinical features

- Encephalopathy
- Jaundice: may be minimal in early stages
- Hepatic foetor
- Liver size: normal or small. Large liver suggests chronicity
- Metabolic acidosis and renal failure may be early and marked in paracetamol overdose
- Coagulopathy
- Hypoglycaemia
- Infection
- Circulatory collapse

## Assessment / monitoring

- **Immediate**: FBC, coagulation screen, blood glucose, U&Es, paracetamol levels, blood and urine cultures.
- **Urgent (within 24 hours)**: LFTs, hepatitis serology (IgM anti-HAV, HBsAg, IgM anti-HBc and anti-HCV).
- Chest x-ray, ultra sound (US) of liver and pancreas.

*Continues on next page*

**Consider:**

- Serum caeruloplasmin, 24 hour urinary copper, Kayser Fleischer rings to be assessed by Ophthalmologist for Wilson's disease.
- Doppler US of hepatic vein if Budd-Chiari suspected.
- EEG if doubt about the aetiology of cerebral dysfunction.

## General management and treatment options

Seek senior help early. ITU admission will be required for all grades of encephalopathy in the acute patient. Your consultant should be aware of the patient on the day of admission so that early discussions can take place with relatives and the Liver Transplant Unit if needed.

### General

- Monitor urine output hourly, blood glucose every 2 hours.
- Do not sedate.
- Avoid arterial puncture (except in paracetamol overdose where a lactate level provides important prognostic information).

### Encephalopathy

- If Grade II or worse on presentation, and cerebral oedema is suspected, nurse 20 - 30$^{O}$ head elevated and give:

  **Mannitol IV 20% , 0.5 g/kg over 30 - 60 minutes and repeat 4 hourly if necessary.**

### Hypoglycaemia

- **Glucose IV 10% at a rate of 100 ml/hour.** For profound hypoglycaemia see guideline on Management of Hypoglycaemia on page 288.
- Continuous infusion of glucose may cause hyponatraemia which may itself be a contraindication to liver transplantation. Therefore the recommendation is to give concurrent:

  **Sodium chloride IV 0.9% plus**

  **Potassium chloride IV 40 mmol/L if hypokalaemic.**

### Coagulopathy

- **Do not** give blood products (i.e. fresh frozen plasma, factor concentrates) unless bleeding is a problem.
- Vitamin K (phytomenadione) does not correct clotting defect but give:

  **Phytomenadione 10 mg slow IV bolus over 3 - 5 minutes to ensure patient is replete.**

**Continues on next page**

**General management and treatment options continued**

## If bleeding occurs

- Discuss with haematologist.
- Take blood for FDPs or D-Dimers to exclude DIC (disseminated intravascular coagulation).
- Give fresh frozen plasma.
- Consider platelets 6 units if platelets < 20 x $10^9$/L.

## Sepsis

- Culture blood and urine at baseline and every 24 hours.

## Renal Failure

- If $K^+$ > 6 mmol/L, $HCO_3^-$ < 15 mmol/L or creatinine > 400 micromol/L, the patient will need renal support. Discuss with renal unit regarding modality.

## Indication for discussion with the Scottish Liver Transplant Unit in Acute Liver Failure

Rather than waiting until the strict criteria for transplantation are met, patients with severe acute liver failure should be discussed with the Scottish Liver Transplant Unit (see Appendix 6 for contact details) at an early stage. This should occur if:

- Prothrombin time > 30 seconds or INR > 2.5
- pH < 7.3 or $H^+$ > 50 nmol/L
- Hypoglycaemia
- Encephalopathy (note encephalopathy may progress rapidly and often manifests as initial mild confusion / disorientation)
- Creatinine > 200 micromol/L
- Raised lactate

## Indications for transplant

The following outlines current indications for transplantation but by the time the patient fulfils the criteria he/she should already be in a liver unit.

**Paracetamol overdose modified Kings (with lactate):**

- Strongly consider listing for transplantation if arterial lactate >3.5 mmol/L after early fluid resuscitation (4 hours).
- List for transplantation if arterial pH < 7.3 or arterial blood lactate >3 mmol/L after adequate fluid resuscitation (12 hours).
- List for transplantation if all three of the following occur within a 24 hour period: creatinine >300 micromol/L, PT > 100 seconds (INR > 6.5), grade ¾ encephalopathy.

Section 4

# Cardiovascular System

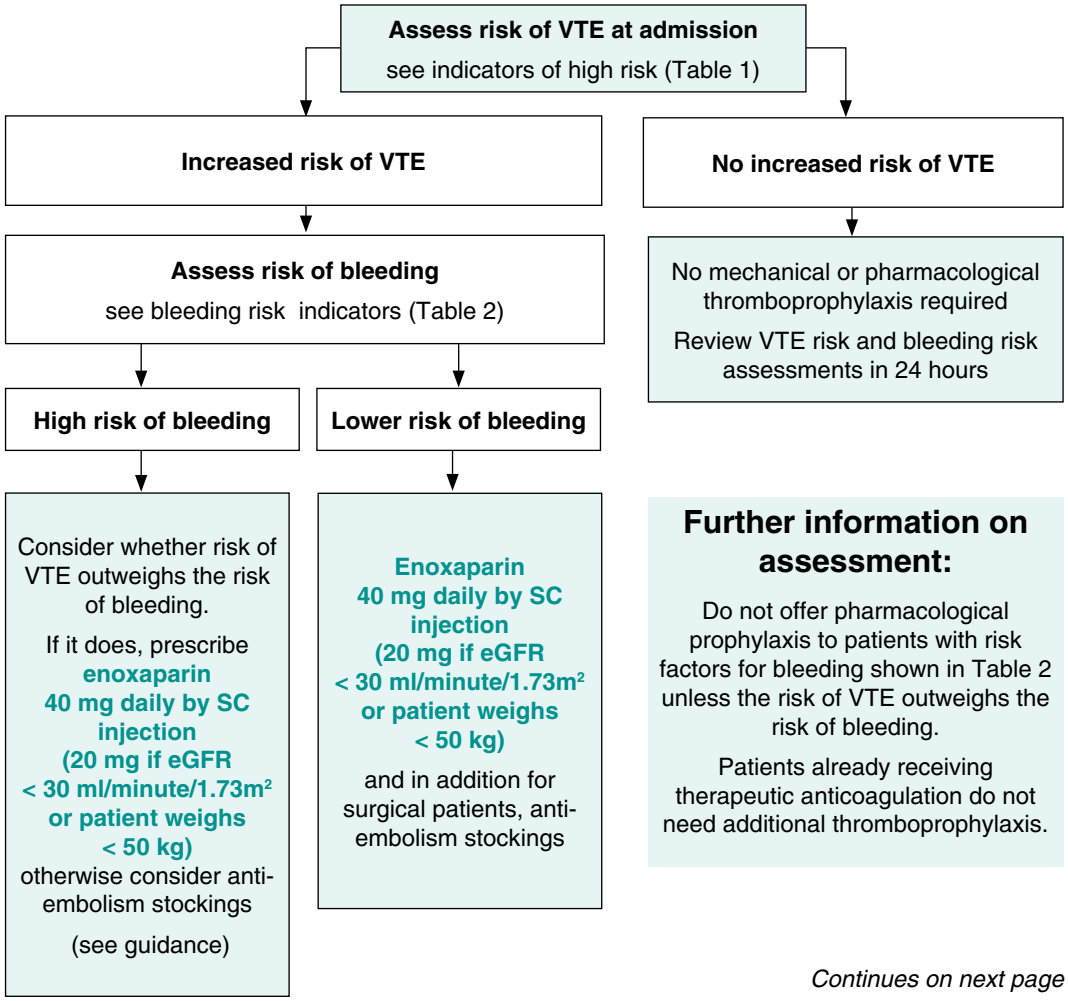
# Thromboprophylaxis for Medical and Surgical Patients

## Assessment of VTE and bleeding risk

All patients must have their risk of venous thromboembolism (VTE) assessed at admission using the appropriate risk assessment tool and then regularly during their stay in hospital. A record of these assessments must be made and documented in the thromboprophylaxis section of the kardex.

Assess the patient at admission using the following algorithm and indicators as guidance and reassess risk of bleeding and VTE within 24 hours of admission and regularly thereafter.

Different specialty specific algorithms apply for orthopaedics, ENT and obstetrics.




### Further information on assessment:

Do not offer pharmacological prophylaxis to patients with risk factors for bleeding shown in Table 2 unless the risk of VTE outweighs the risk of bleeding.

Patients already receiving therapeutic anticoagulation do not need additional thromboprophylaxis.

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**Table 1 – Indicators of patients at increased risk of VTE**

Regard medical patients as being at increased risk of VTE if they are expected to have ongoing (≥ 2 days) reduced mobility relative to their normal state **and** have one or more of the risk factors below. Regard surgical patients as being at increased risk of VTE if they have one or more of the following risk factors:

- Acute surgical admission with inflammatory or intra-abdominal condition
- Dehydration
- Critical care admission
- Surgical procedure with total anaesthetic/ surgical time > 90 min, or > 60 min if surgery on lower limb
- Age > 60 yrs
- Obesity (BMI > 30 kg/m$^2$)
- Active cancer
- Thrombophilia
- Personal history or 1st degree relative with a history of VTE
- Hip fracture
- Current significant medical condition e.g.
  - Serious infection
  - Heart failure
  - Respiratory disease
  - Inflammatory disease
- Pregnancy or ≤ 6 weeks post partum **(seek specialist advice)**
- Hormone replacement therapy, tamoxifen
- Oestrogen containing contraceptive pill
- Varicose veins with phlebitis

This list is not comprehensive and there will be patients with other specific conditions which are sufficiently pro-thrombotic that merit thromboprophylaxis.

**Table 2 – Indicators of patients at high risk of bleeding**

Regard patient at risk of bleeding if they have any of the following risk factors:

- Surgery expected within next 12 hours
- Surgery within past 48 hours and/or risk of clinically important bleeding
- Active bleeding or risk of bleeding including
  - new-onset stroke
  - platelet count < 75 x 10$^9$/L
  - acute liver failure
- Concurrent use of therapeutic anticoagulant
- Acute bacterial endocarditis
- Any spinal intervention (prophylactic enoxaparin dose is contraindicated for 12 hours before spinal and epidural anaesthetics and lumbar puncture. Enoxaparin contraindicated for 4 hours after spinal and epidural anaesthetics and removal of epidural catheter)
- Persistent uncontrolled hypertension (BP ≥ 230/120 mmHg)
- Untreated inherited bleeding disorder (e.g. haemophilia or von Willebrands)
- Neurosurgery, spinal, posterior eye or thyroid surgery

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## General management and treatment options

Surgical patients who merit pharmacological thromboprophylaxis should receive:

- **Enoxaparin SC 40 mg daily (at 6 pm) and anti-embolic stockings**

Medical patients who merit pharmacological thromboprophylaxis should receive:

- **Enoxaparin SC 40 mg daily (at 6pm) only.**

**N.B. Reduce the dose of enoxaparin to 20 mg SC once daily if eGFR < 30 ml/minute/1.73m$^2$. It may be appropriate to reduce dose to 20 mg in patients of low weight (< 50 kg).**

Extremely heavy patients (> 120 kg), with normal renal function, may merit higher doses of enoxaparin (see StaffNet, Clinical Guideline Electronic Resource Directory and search in 'Haematology' section).

Enoxaparin should only be prescribed after assessing the risks of VTE and balancing against the risks of bleeding.

Contraindications should be considered carefully (e.g. Heparin induced Thrombocytopaenia (HIT), acute bacterial endocarditis, recent stroke, etc).

### Timing of enoxaparin administration

For medical in-patients enoxaparin should be prescribed at 6 pm. For surgical in-patients with a significant reduction in mobility enoxaparin should be prescribed at 6 pm the night before surgery. Otherwise it should be started after surgery at the later of: 4 hours post-operatively or 6 pm. Then at 6 pm on subsequent days.

### Same day admission surgery

Compared to inpatient surgery, day case surgery generally confers a lower (but not zero) VTE risk. Therefore these patients should be similarly risk assessed for VTE and bleeding risk, and if appropriate AES and LMWH prescribed. In patients perceived to be at very high VTE risk, consideration can be given to extending LMWH prophylaxis post discharge.

For patients admitted on the day of surgery who require enoxaparin thromboprophylaxis:

- Anti-embolic stockings at admission
- Enoxaparin started after surgery at the later of: 4 hours post-operatively or 6 pm. Then at 6 pm on subsequent days.

### Precautions with epidural and spinal anaesthetic techniques

Epidural and spinal anaesthetic techniques should not be carried out within 12 hours of a prophylactic dose of enoxaparin. Likewise epidural catheters should not be removed within 12 hours of a prophylactic dose of enoxaparin. Wait > 4 hours after any of these procedures before giving next dose of enoxaparin. In most cases administration of enoxaparin at 6 pm will avoid any difficulties here.

### Monitoring platelet count

All patients prescribed heparin, including LMWH, should have a baseline platelet count assessed. Heparin induced thrombocytopenia (HIT) is most commonly seen in post-operative patients receiving unfractionated heparin (UFH). Post-operative patients receiving UFH and post cardio-pulmonary bypass (CPB) patients receiving UFH or LMWH should have platelet count monitoring every 2-3 days from days 4 to 14 or until heparin is stopped.

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If the platelet count falls to < 100 x$10^9$/L, or if there is a smaller but significant drop (30 - 50%) from baseline, stop the heparin and seek specialist advice. Medical and obstetric patients receiving UFH or LMWH, and post-operative patients (excluding post-CPB patients) receiving LMWH, have a low risk of HIT and do not require routine platelet count monitoring for this purpose. Further advice on Diagnosis and Treatment of HIT can be found in StaffNet, Clinical Guideline Electronic Resource Directory and search in 'Haematology' section.

## Anti-embolism stockings (AES)

- Sigel profile compliant AES should be used.
- Calf length AES may be used where thigh length AES are unsuitable.
- AES may be replaced with intermittent pneumatic compression devices (IPC) whilst in hospital.
- AES must be removed for 30 minutes in each 24 hour period.
- Reassess daily for any changes to skin or changes to patient's condition such as oedema, and re-measure if any changes noted.
- Medical practitioners must prescribe the use of AES within the medication kardex.

*Incorrect fitting of AES can be detrimental to the patient causing skin damage*. Observation and continual assessment is required.

| Do not offer AES to patients who have: | Cautions |
|---|---|
| Peripheral arterial disease | Ensure the correct size is provided |
| Peripheral neuropathy of legs | Re-measuring and refitting may be required |
| Leg / foot ulcers | Ensure good capillary refill after fitting |
| Fragile 'tissue paper' skin | Show patients how to use AES |
| Major limb deformity | Ensure patients discharged with AES are able to remove and replace them (or have assistance) |
| Cellulitis or massive oedema | Do not fold down the tops of AES |

# Duration of thromboprophylaxis

- AES – continue until patient discharged and returned to pre-admission level of mobility.
- Enoxaparin – usually stopped at discharge, or earlier if patient no longer at high thrombotic risk when re-assessed.
- Extended anticoagulant thromboprophylaxis is indicated in specific patients (e.g. known high risk thrombophilia or previous post-op VTE, but not on long-term warfarin) or situations (e.g. post abdomino-pelvic cancer surgery or THR).

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## General recommendations

- Facilitate early mobilisation as soon as possible.
- Do not allow patients to become dehydrated.
- Advise patients to consider stop taking oestrogen-containing oral contraceptives or hormone replacement therapy before elective surgery and establish suitable alternative contraception.
- Pre-existing established anti-platelet therapy:
  - Assess risks and benefits of stopping before surgery.

    See NHSGGC Secondary Prevention of Coronary Heart Disease – Antiplatelet Guideline, page 100 and antiplatelet guidance following stroke, page 124.
  - Do not regard low dose antiplatelet therapy as adequate prophylaxis for VTE.
  - Consider offering additional VTE prophylaxis to patients taking antiplatelet agents assessed to be at increased risk of VTE ( Table 1), taking into account the increased risk of bleeding.
- Pre-existing established warfarin therapy
  - See NHSGGC Management of Patients on Anticoagulant Therapy in the Perioperative Period guideline (page 88).
  - Do not offer enoxaparin to those on full anticoagulant therapy.
- If regional anaesthesia is used, pharmacological prophylaxis must be timed to minimise the risks of epidural haematoma.

# Diagnosis and Treatment of Venous Thromboembolism

For suspected VTE in pregnant patients, refer to separate guideline on page 80.

## Introduction

Fifty percent of Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE) arise spontaneously, without any obvious triggering event; there are many risk factors which are particularly common in hospitalised patients.

Early recognition and treatment of an acute venous thromboembolism (VTE) is essential to reduce the risk of early fatal PE. It is estimated that deaths from hospital acquired PE far exceed those from hospital acquired infection.

## Diagnosis of acute VTE

**Signs and symptoms which may accompany an acute DVT or PE include:**

- Calf warmth, tenderness, swelling, pitting oedema, erythema
- Chest pain (often pleuritic), cyanosis, breathlessness, haemoptysis, collapse
- Tachycardia / hypotension, raised JVP, hypoxia, tachypnoea

In almost all suspected cases positive radiological confirmation will be required. However, for those presenting from the community it may be possible to rule out such a diagnosis by use of pre-test clinical probability scoring schemes in conjunction with measurement of fibrin D-dimer levels, which are almost invariably increased in cases of acute VTE (see decision algorithms pages 72 - 74). D-Dimer measurement is not useful in the diagnosis of VTE in pregnant women or already hospitalised patients and should **not** be measured in these patient groups.

**If DVT or PE is not excluded by the above, or the patient is already hospitalised then:**

- Check baseline coagulation screen, FBC, U&Es and LFTs.
- Unless contraindicated, commence anticoagulant therapy with low molecular weight heparin (LMWH) – see page 75, Drug therapy / treatment options section.
- Arrange objective radiological imaging (e.g. compression ultrasound leg or CTPA chest or V/Q lung scan).

## Diagnosis and early management of suspected massive PE

Brief guidance is given below. Full guidance on the diagnosis and early management of a suspected massive PE can be found on StaffNet, Clinical Guideline Electronic Resource Directory and search in the 'Haematology' section.

### Definition of massive PE

PE associated with a systolic blood pressure < 90 mmHg or a drop in systolic blood pressure of ≥ 40 mmHg from baseline for a period >15 minutes (not otherwise explained by hypovolaemia, sepsis or new arrhythmia)

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## Initial management

- Seek immediate senior advice as patient may need transfer to CCU / ICU / HDU / Resus
- Heparinise with IV unfractionated heparin bolus (5,000 units) then IV infusion (18 units/kg/hour adjusted to maintain APTT ratio of 1.8 - 2.8) - see page 76.
- Perform urgent CTPA or cardiac ECHO (if CTPA not possible / not available)
- $O_2$
- IV fluids and inotropic support
- If pregnant, inform on-call obstetric team immediately for consideration of early delivery
- If there is persistent hypotension (SBP < 90 mmHg) and either CTPA confirms PE, cardiac ECHO demonstrates RV dilatation / dysfunction or patient is in peri-arrest, then consider thrombolysis as follows:
  - Alteplase IV 10 mg over 1 - 2 minutes followed by 90 mg over 2 hours (max 1.5 mg/kg if < 65 kg); if this is not available, consider using local regimen for MI (unlicensed for PE).
  - Continue heparin to maintain APTT ratio 1.8 - 2.8

If thrombolysis contraindicated, consider percutaneous catheter fragmentation or surgical embolectomy. Be aware that when considering thrombolysis the risk of major haemorrhage is significantly increased in the older patient.

## Diagnostic algorithm for out-patients with suspected DVT

Patients with chronic heart failure or suspected bilateral DVT and patients at extremes of weight or with renal impairment (i.e. CrCl < 30 ml/minute) preventing the safe use of LMWH, may not be suitable for out-patient investigation and management of suspected VTE.

**Table 1 – Wells Clinical Score**

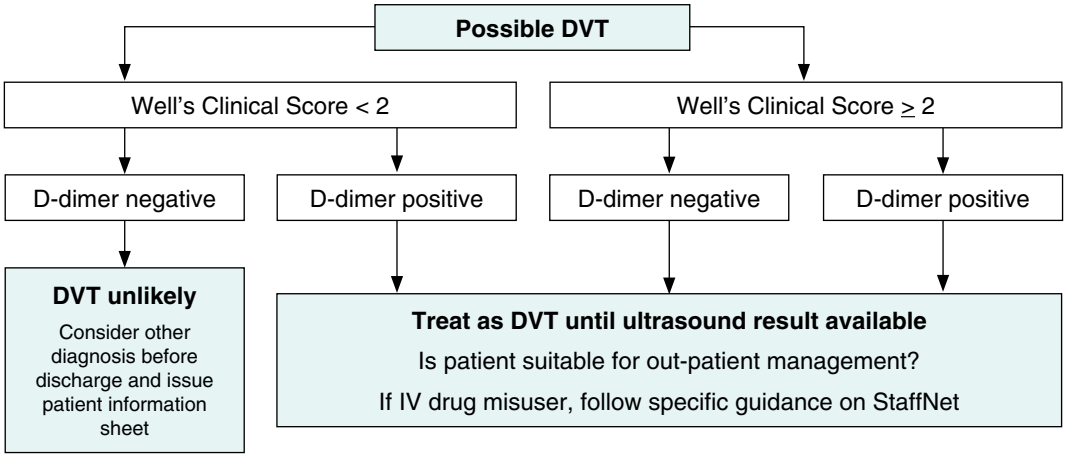
| | |
|---|---|
| Active cancer (treatment ongoing, within previous 6 months or palliative) | 1 |
| Paralysis, paresis or recent plaster immobilisation of lower extremities | 1 |
| Recently bedridden for ≥ 3 days or major surgery within 12 weeks | 1 |
| Localised tenderness along distribution of deep venous system | 1 |
| Entire leg swollen | 1 |
| Calf swollen by ≥ 3 cm compared to asymptomatic leg (10 cm below tibial tuberosity) | 1 |
| Pitting oedema (greater in symptomatic leg) | 1 |
| Collateral superficial veins (non-varicose) | 1 |
| Previously documented DVT | 1 |
| Alternative diagnosis as likely or greater than that of DVT | -2 |
| TOTAL: | |

*Score < 2: DVT unlikely  Score ≥ 2: DVT possible*

From The New England Journal of Medicine, Philip S. Wells, David R. Anderson, Marc Rodger, et al., Evaluation of D-Dimer in the Diagnosis of Suspected Deep-Vein Thrombosis, 349(13), 1227-35. Copyright © (2013) Massachusetts Medical Society. Adapted with permission from Massachusetts Medical Society.

*See flow chart on next page*

**Wells Clinical score should be utilised in all NHSGGC hospitals when DVT is suspected in out-patients**




Out-patients who have a negative ultrasound should be considered for a repeat scan at 5 -7 days if there is no likely alternative diagnosis for their leg symptoms.

## Diagnostic algorithm for out-patients with suspected PE

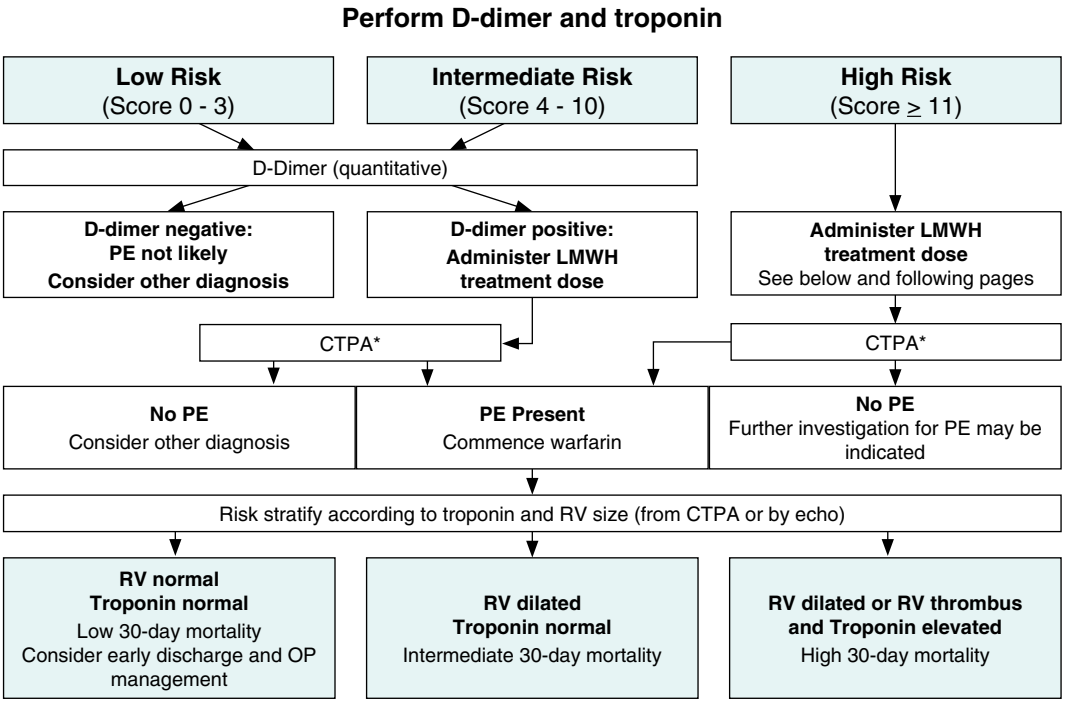
- Assess predictive risk score using following scoring tool
- Identify risk of PE and follow guidance in flow-chart
- If patient is haemodynamically unstable consider massive PE and refer to guidance on page 71 and the full guideline on StaffNet.

**Table 2 – Modified Geneva Predictive Risk Score**

| | |
|---|---|
| Age > 65 years | 1 |
| Previous DVT / PE | 3 |
| Recent surgery or recent lower limb fracture (≤ 1 month) | 2 |
| Malignant disease (active or cured ≤ 1 year) | 2 |
| Unilateral lower limb pain | 3 |
| Haemoptysis | 2 |
| Heart rate 74 - 94 bpm | 3 |
| Heart rate ≥ 95 bpm | 5 |
| Pain on deep venous palpitation of leg and unilateral oedema | 4 |
| TOTAL: | |

Le Gal G, Righini M, Roy PM, et al. (February 2006). Prediction of pulmonary embolism in the emergency department: the revised Geneva score. Annals of Internal Medicine 144(3); 165-171. Copyright © 2013 The American College of Physicians. All Rights Reserved. Adapted with permission from The American College of Physicians.

*See flow chart on next page*




*If CTPA is not readily available and patient is clinically stable with normal CXR and no underlying lung disease, then V/Q scan may be an alternative diagnostic option.

Full guidance is available in the Clinical Guideline Electronic Resource Directory on StaffNet.

# General Management

Aim to provide therapeutic anticoagulant therapy for 3 - 6 months (or indefinitely for some patients with life-threatening or recurrent thrombosis), normally using LMWH initially followed by oral warfarin (with an overlap of at least 5 days). Oral rivaroxaban, for 3 - 6 months, is an acceptable alternative for patients with acute DVT or PE, see page 79.

### Special cases where management may differ include:

**Pregnant patients**

- Both diagnostic and management strategies differ (see page 80).

**Patients with active cancer**

- These patients should be managed with LMWH only, due to high risk of bleeding and risk of early recurrent thrombosis. Seek advice and discuss with patient and their cancer team. Full guidance is available on StaffNet, Clinical Guideline Electronic Resource Directory and search in the 'Haematology' section.

**Patients with superficial thrombophlebitis**

Some patients with extensive superficial thrombophlebitis proximal to the knee can be considered for 6 weeks of anticoagulation with prophylactic dose LMWH (i.e. **enoxaparin 40 mg once daily**). A full guideline pertaining to this management will be available on StaffNet, Clinical Guideline Electronic Resource Directory and search in the 'Haematology' section.

**IV Drug Misusers**

- Given their chaotic lifestyles and habits, these patients may be considered at high risk of bleeding complications from therapeutic anticoagulant therapy, particularly warfarin therapy which demands careful compliance with monitoring and avoidance of interacting drugs (including alcohol).
- For these patients an individualised risk / benefit assessment is required, and there are three possible approaches to outpatient management of DVT in these patients:
  1. No anticoagulant therapy
  2. LMWH or oral rivaroxaban for 6 weeks
  3. Warfarin or rivaroxaban treatment for 3 - 6 months

An algorithm to inform the decision as to which treatment option is the most suitable and with details of treatment for related conditions (e.g. cellulitis) is available on StaffNet, Clinical Guideline Electronic Resource Directory and search in the 'Haematology' section.

**Screening for cancer in patients with unprovoked venous thrombosis**

In patients over 40 years old, who have no 'red flag' signs for cancer that might warrant specific targeted investigations, undertake screening urinalysis and CXR. Mammogram, in women, and CT abdomen and pelvis may be considered in high risk cases.

**Thrombophilia testing**

Thrombophilia testing is warranted in some patients who experience a VTE but should **not** be performed at the time of the acute event or during anticoagulation therapy.

## Drug therapy / treatment options

**Subcutaneous LMWH** (see pages 80 - 82 for dosing in pregnant patients)

Dalteparin is the LMWH of choice across NHSGGC for the initial treatment of VTE unless the patient is pregnant or has specific contraindications to dalteparin (although some patients with acute PE and/or DVT may be considered for oral rivaroxaban) and most patients with cancer should continue treatment with LMWH for the duration that anticoagulation is required.

**Continue with dalteparin until:**

- The diagnosis is disproved **or**
- The diagnosis is confirmed and either rivaroxaban is commenced or dalteparin has been over-lapped with warfarin for at least 5 days and the INR has been $\geq$ 2 for two consecutive days.
- Dalteparin does not require laboratory monitoring (APTT is inappropriate, though if significant renal impairment or exceptionally low or high BMI, consider assessing anti-factor Xa activity after 2 - 3 consecutive doses of dalteparin, at 4 hours post dose (when target would be 0.5 - 1 units/ml)). Guidelines on appropriate use of LMWH at extremes of body weight and with renal impairment (CrCl < 30 ml/minute) are available on StaffNet, Clinical Guideline Electronic Resource Directory and search in the 'Haematology' section..

**Continues on next page**

**Drug therapy / treatment options continued**

## Dalteparin

Dose is 200 units/kg subcutaneously once daily. 18,000 units is the maximum recommended daily dose.

**Table 3 – Dalteparin dosing**

| Actual weight (kg) | Dalteparin daily dose (units) using pre-filled syringes | Dalteparin Syringe Colour |
|---|---|---|
| 34 - 45 | 7,500 | Green |
| 46 - 56 | 10,000 | Red |
| 57 - 68 | 12,500 | Orange |
| 69 - 82 | 15,000 | Purple |
| ≥ 83 | 18,000 | White |

**NOTES**

- Guidance on heparin dose adjustment for patients with significant renal impairment or weighing > 120 kg are available in the Clinical Guideline Electronic Resource Directory on StaffNet.
- If there is concern about efficacy in patients weighing > 95 kg, anti-factor Xa activity should be checked after 2-3 consecutive doses of dalteparin, at 4 hours after a dose.
- Lower doses of dalteparin should be considered in patients with significant liver and/or renal failure (CrCl < 30 ml/minute).

## Unfractionated Heparin (Sodium Heparin)

- Used in treatment of DVT / PE if rapid anticoagulation is deemed appropriate (e.g. massive PE) or patients thought to be at particularly high bleeding risk (e.g. recent surgery/trauma)
- There are different concentrations of unfractionated heparin currently available - only the 1000 units/ml preparation should be used at all times
- LOADING DOSE: 5,000 units by IV bolus over 5 minutes - use one 5 ml vial of 1000 units/ml (total concentration 5000 units/5 ml)
- MAINTENANCE INFUSION: 18 units/kg/hour (usually ~ 1,200 units (1.2 ml) per hour for a 70 kg patient). If patient is at high risk of bleeding, start at 1000 units/hour. Use one 20 ml vial of 1000 units/ml (total concentration 20,000 units/20 ml). Replace the syringe at least every 24 hours, until treatment is discontinued.
- Monitoring – Check APTT ratio after 6 hours and 4 hours after any change in infusion rate, then daily.
- Adjust infusion rate according to APTT ratio (see table on next page).

**Continues on next page**

**Drug therapy / treatment options continued**

**Table 4 – Unfractionated heparin dose adjustment**

| APTT ratio | Sodium Heparin Infusion Rate Change |
|---|---|
| > 4.0 | Stop for 60 minutes and recheck APTT ratio, before recommencing at a rate reduced by 300 - 500 units/hour |
| 3.5 - 4.0 | Stop for 60 minutes and reduce heparin by 200 units/hour |
| 2.9 - 3.4 | Stop for 30 minutes and reduce heparin by 100 units/hour |
| 1.8 - 2.8 | No change |
| 1.2 - 1.7 | Increase heparin by 200 units/hour |
| < 1.2 | Increase heparin by 400 units/hour and consider further bolus of 5,000 units heparin |

**NOTES**

- Rarely should patients require infusion rates > 1.6 - 2 ml/hour. If target APTT ratio of 1.8 - 2.8 is not being achieved with a dose of 1.6 ml/hour, then monitor anti-factor Xa level (target 0.35 - 0.7 units/ml).
- Routine platelet count monitoring for Heparin Induced Thrombocytopenia is not required unless **unfractionated heparin** is being administered within 3 months of recent surgery.

## Warfarin

- Used as follow-on from LMWH in intermediate and long-term treatment of DVT and PE (except in pregnant patients and some IVDU and cancer patients).
- Induction treatment with warfarin should always follow a validated induction dosing algorithm suitable to the patient, and be accompanied by INR testing on the specified days.
- The following algorithm (age-adjusted Fennerty regimen) is suitable for most inpatients who require to quickly achieve a therapeutic INR of 2 - 3. Daily INR testing is required with this algorithm.
- The use of alternative 'slower' induction regimens (with less intense monitoring) should be considered in outpatients and the elderly (see StaffNet for acceptable alternative induction regimens).
- Warfarin should be administered orally, once daily at 6 pm.

**Continues on next page**

## Warfarin flexible induction regimen (Age-adjusted Fennerty)

***N.B.*** *The table below gives dosing advice for the first 4 days of warfarin initiation only. It is not appropriate for dosing from day 5 onwards which should be undertaken manually using clinical judgement.*

**On initiation:**

- Perform baseline INR (unless part of initial coagulation screen), and repeat INR daily on the first 4 days.
- When the INR result is towards the upper end of a range in the INR column, it is recommended that a warfarin dose is chosen towards the lower end of the suggested range in the age-appropriate dose column; and vice versa when INR result is towards the lower end of an INR range.
- Beyond day 4 dosage adjustment may still be required, especially between days 5 and 14 when INR may need to be assessed every 2 - 3 days until stable and patient has been transferred to an appropriate outpatient INR monitoring service (see page 83).
- More careful dosing and monitoring may be required in elderly patients or where there is co-administration with drugs known to increase or decrease INR (consult BNF or seek advice from clinical pharmacists).

**Table 5 – Warfarin age-adjusted induction regimen**

| Day | INR | Dose for age (mg) | | | |
|---|---|---|---|---|---|
| | | ≤ 50 yr | 51 - 65 yr | 66 - 80 yr | > 80 yr |
| 1 | < 1.4 | 10 | 9 | 7.5 | 6 |
| 2 | < 1.6 | 10 | 9 | 7.5 | 6 |
| | ≥ 1.6 | 0.5 | 0.5 | 0.5 | 0.5 |
| 3 | < 1.8 | 10 | 9 | 7.5 | 6 |
| | 1.8 - 2.5 | 4 - 5 | 3.5 - 4.5 | 3 - 4 | 2.5 - 3 |
| | 2.6 - 3.0 | 2.5 - 3.5 | 2.5 - 3.5 | 2 - 2.5 | 1.5 - 2 |
| | 3.1 - 3.5 | 1 - 2 | 1 - 2 | 0.5 - 1.5 | 0.5 - 1.5 |
| | 3.6 - 4.0 | 0.5 | 0.5 | 0.5 | 0.5 |
| | > 4 | 0 | 0 | 0 | 0 |
| 4 | < 1.6 | 10 - 15 | 9 - 13 | 7.5 - 11 | 6 - 9 |
| | 1.6 - 1.9 | 6 - 8 | 5.5 - 7 | 4.5 - 6 | 3.5 - 5 |
| | 2.0 - 2.6 | 4.5 - 5.5 | 4 - 5 | 3.5 - 4.5 | 2.5 - 3.5 |
| | 2.7 - 3.5 | 3.5 - 4 | 3 - 3.5 | 2.5 - 3 | 2 - 2.5 |
| | 3.6 - 4.0 | 3 | 2.5 | 2 | 1.5 |
| | 4.1 - 4.5 | Omit today's dose and on day 5 give the following dose (if INR < 4.1): | | | |
| | | 1 - 2 | 0.5 - 1.5 | 0.5 - 1.5 | 0.5 - 1 |
| | > 4.5 | Withhold warfarin until INR back between 2.0 - 3.0 (then restart on 0.5 - 1mg) | | | |

G. W. Roberts, T. Druskeit, L. E. Jorgensen, L. M. H. Wing, A. S. Gallus, C. Miller, D. Cosh, V. S. Eaton. Comparison of an age adjusted warfarin loading protocol with empirical dosing and Fennerty's protocol. Aust NZ J Med 1999; 29; 731-736. Copyright © 2013 John Wiley and Sons. Adapted with permission from John Wiley and Sons.

**Decrease dose by 33% if the patient has one or more of the following risk factors:**

- Severe congestive cardiac failure (EF < 30% and/or biventricular failure)
- Severe COPD (oxygen or steroid dependent or dyspnoea at rest)
- Concurrent treatment with amiodarone

## Rivaroxaban

Rivaroxaban is an oral direct factor Xa inhibitor which has been shown to be as effective as LMWH followed by warfarin in the treatment of acute PE and/or DVT. However, there is limited experience of treating PE or DVT patients for longer than 12 months. No monitoring of the anticoagulant effect of rivaroxaban is required, and although it has a short half-life, rivaroxaban has no reversing agent.

Rivaroxaban may be regarded as a suitable alternative to LMWH followed by warfarin in patients with acute DVT for whom the intended duration of anticoagulation (at the outset) is determined to be 3 or 6 months. Where treatment duration is planned to be indefinite, then warfarin remains the preferred treatment of choice.

### Patients with acute PE and/or DVT deemed suitable for rivaroxaban therapy:

- Should be treated with LMWH (dalteparin) until the diagnosis has been objectively confirmed.
- Rivaroxaban use is not recommended if CrCl is < 15 ml/minute, and should be used with caution if CrCl is 15 - 29 ml/minute.
- Start rivaroxaban 22 - 24 hours after the last dose of dalteparin.
- Give **rivaroxaban oral 15mg twice daily for the first three weeks and then 20 mg once daily for the remaining duration of treatment (i.e. 3 or 6 months).**

  In renal impairment (CrCl 15 - 49 ml/minute) reduce **rivaroxaban dose from day 22 onwards to 15 mg once daily in patients perceived to be at high risk of bleeding**. In patients with CrCl of 15 - 29 ml/minute, rivaroxaban plasma concentrations are significantly increased, therefore, it should be used with caution in these patients

### Exclusion for rivaroxaban treatment include:

- Creatinine clearance <15 ml/minute
- Liver disease associated with cirrhosis or coagulopathy
- Pregnancy or breast feeding
- Concurrent therapy with azoles (except fluconazole), protease inhibitors or strong CYP3A4 inducers (e.g. rifampicin, phenytoin)
- Patients perceived to be at high bleeding risk who would not be suitable for any therapeutic anticoagulant therapy.

### Patients being discharged on rivaroxaban:

- The initial 21 days of treatment (15mg twice daily) should be provided from hospital pharmacy.
- Patients on rivaroxaban do not require referral to an anticoagulant clinic.
- The GP copy of the patient discharge medications should be accompanied with clear written information for the GP regarding the ongoing time-restricted prescription of this medication and its important contraindications.
- Any patient commenced on rivaroxaban should be issued with a Rivaroxaban Patient Alert card and offered counselling about this anticoagulant medication.

# Prevention and Management of Venous Thromboembolism in Pregnancy

The full guideline on 'The Management of Acute Thromboembolic Disease in Pregnancy' is available via StaffNet / Acute / Women and Children's Services / Obstetrics / GGC obstetric guidelines.

## Introduction

Venous thromboembolism (VTE) is a major cause of maternal death in the United Kingdom. Clinical assessment and diagnosis of women presenting with suspected VTE in pregnancy is unreliable and clinical suspicion must always be confirmed by appropriate objective testing. The signs and symptoms of VTE include: leg pain and swelling (usually unilateral), lower abdominal pain, low grade pyrexia, dyspnoea, chest pain, haemoptysis and collapse.

In prophylaxis of VTE in pregnancy enoxaparin or tinzaparin is used. **Before** initiating prophylactic therapy, seek specialist advice to discuss doses and monitoring during pregnancy.



## Prevention of VTE in pregnancy

- Assessment of risk factors for VTE is usually made at booking, throughout pregnancy and in the postnatal period (see full guideline on StaffNet for details on risk factors).
- Thrombophilia screen at booking should be considered in women with either:
  - a family history of both VTE and thrombophilia **or**
  - a family history of VTE in a 1st degree relative which was unprovoked or provoked by a minor risk factor (e.g. hormone-related [including pregnancy], minor trauma or long distance travel).
- Women with a personal history of VTE which was unprovoked or provoked by a minor risk factor (as above) should be tested for antithrombin deficiency only, as this is the only inherited thrombophilia which, if present, could alter management during pregnancy – see Thrombophilia Testing Guideline on StaffNet.
- Women with ***several risk factors for VTE*** may require antithrombotic therapy antenatally and/or postnatally: anti-embolism stockings, low molecular weight heparin (LMWH) or unfractionated heparin (see full guideline on StaffNet / Acute / Women and Children's Services / Obstetrics / GGC obstetric guidelines).

## Investigation of suspected VTE

- Send for FBC, U&Es, coagulation screen, LFTs.
- After checking patient's bloods and whilst awaiting results of diagnostic tests (as outlined on the next page) commence anticoagulation therapy (see Drug therapy / treatment options section of this guideline).

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### Diagnosis of VTE in pregnancy

- If Deep Vein Thrombosis (DVT) is suspected:
  - Compression Duplex ultrasound is the primary diagnostic test. If ultrasound confirms DVT diagnosis then continue anticoagulating.
  - If ultrasound is negative but a high level of clinical suspicion remains, the patient should remain anticoagulated and ultrasound repeated in one week or an alternative diagnostic test employed. If repeat testing is negative, anticoagulant treatment should be discontinued.
  - When iliac vein thrombosis is suspected, (back pain and swelling of the entire limb) magnetic resonance venograph or conventional contrast venography may be considered.
- If Pulmonary Embolism (PE) is suspected:
  - Perform chest x-ray. This may provide a reason for the chest symptoms. An electrocardiograph is rarely helpful and pulse oximetry is often more useful and safer than arterial blood gases.
  - If the chest x-ray is normal, PE is still suspected and there are symptoms and/or signs of DVT then leg Doppler scans should be performed. If these show a DVT, anticoagulant treatment should be continued and further radiological investigations are not required.
  - If the chest x-ray is normal, PE is still suspected and there are **no** symptoms and/or signs of DVT, then a ventilation / perfusion scan (V/Q scan) or CT-pulmonary angiography (CTPA) should be performed. V/Q scanning is first line investigation for suspected PE in all maternity units within NHSGGC. If the patient has an abnormal chest x-ray or is unstable, a CTPA is the investigation of choice.
- If a V/Q scan or CTPA is required, the woman should be counselled with regard to the risk of radiation exposure both to her and her unborn baby.
- Testing for D-dimer and performing a thrombophilia screen in the acute situation, should not be performed.

## General management

Following DVT, fitted European Grade II graduated elastic compression stockings (23 - 32 mmHg) should be worn on the affected leg for up to 2 years.

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# Drug therapy / treatment options

## Treatment of VTE in pregnancy

1. Start treatment with a LMWH:

**(i) Initial dose of enoxaparin is determined as follows:**

| Early pregnancy weight | Initial dose of enoxaparin |
|---|---|
| < 50 kg | 40 mg twice daily |
| 50 - 69 kg | 60 mg twice daily |
| 70 - 89 kg | 80 mg twice daily |
| > 90 kg | 100 mg twice daily |

**(ii) Initial dose of tinzaparin: 175 units/kg once daily. Use early pregnancy weight.**

2. Monitor LMWH therapy

   Routine measurement of peak anti-factor Xa activity for patients on LMWH for treatment of acute VTE in pregnancy or post-partum is not recommended but can be requested if:

   - Obstetric patient is at extremes of body weight (< 50 kg and ≥ 90 kg).
   - Obstetric patient has other complicating factors which puts her at high risk (e.g. renal impairment, recurrent VTE).

3. Platelets - obstetric patients receiving LMWH or UFH (unless UFH post-op) do not require routine platelet monitoring for Heparin Induced Thrombocytopenia..
4. Continue full dose LMWH throughout pregnancy.
5. Labour, caesarean section, and regional anaesthesia – inform the on-call obstetric team of this patient and see the full guideline on StaffNet for details..
6. High risk of haemorrhage - discuss patient with specialists and also refer to the full guideline on StaffNet..
7. Postnatal anticoagulation

   Anticoagulant therapy should be continued for the duration of the pregnancy and for at least 6 weeks postnatally and until **at least** 3 months of treatment has been given in total. Refer to full guideline on StaffNet for information regarding postnatal treatment choice.

   Patients developing VTE in pregnancy should be referred to the haematology clinic or obstetric medical / haematology clinic for follow up investigations (including thrombophilia testing, if appropriate, once heparin treatment has been discontinued) and anti-factor Xa activity if appropriate.

# Referral of Patients to Anticoagulant Clinic

Patients being discharged from hospital on warfarin will usually be in an unstable phase of anticoagulation. It is therefore essential that the transition of anticoagulant monitoring from hospital care to the community or outpatient clinic is well organised and clearly documented for the patient and clinical staff involved.

## Anticoagulant service providers

Within NHSGGC all community INR monitoring services are provided by the Glasgow and Clyde Anticoagulation Service (GCAS), rather than individual GPs (who should not be asked to undertake routine INR monitoring). See Appendix 6 for GCAS contact details.

The GCAS Anticoagulant Monitoring and Clinic referral form contains all necessary information and other contact details – see StaffNet.

For patients resident outwith NHSGGC, please contact patient's GP to identify the most appropriate anticoagulant service for the patient.

## Prior to discharge

Key recommendations are as follows:

- Ensure an anticoagulant clinic appointment is made for the patient (usually for 3 - 7 days following discharge, unless patient is stably anticoagulated when their appointment should be no longer than 2 weeks post discharge).
- Ensure transport is booked and confirmed for this appointment, if required.
- Issue patient with a yellow anticoagulant booklet and ensure it is fully completed. It must contain the patient's details and include the 3 most recent INR results and resulting warfarin doses (including dose at discharge) so as to allow safe dosing at their first anticoagulant clinic visit.
- Record the date, time and venue for the patient's next anticoagulant clinic appointment in the yellow booklet.
- Fax a fully completed copy of the Glasgow and Clyde Anticoagulant Service (GCAS) Anticoagulant Monitoring and Clinic Referral form which includes recent INR results and resulting warfarin doses to the GCAS team - fax numbers are included at the bottom of the form. A copy of this form should then be handed to the patient to take to their first anticoagulant clinic appointment.
- Educate the patient on their anticoagulant therapy (indication for treatment, interacting factors and bleeding risks), ensure they know how to take their anticoagulant medications and arrange a suitable supply of them.

If a patient is unable to attend an anticoagulation clinic on discharge this should be discussed further with the relevant anticoagulant service provider. Within Glasgow and Clyde this will usually be the Lead Nurse for the Glasgow and Clyde Anticoagulant Service (GCAS), and not the GP (see Anticoagulant Monitoring and Clinic Referral form for contact details).

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## Patients recently commenced on warfarin (new patients)

Such patients should be referred to their local anticoagulant service provider (this will usually be the GCAS service) using the Anticoagulant Monitoring and Clinic Referral form. Patients living out with NHSGGC should be referred to their GP. Complete the referral form fully and include the following details:

- Full patient and GP details and contact information.
- Details of referring consultant and location.
- Indication for warfarin, target INR and intended duration of treatment.
- Recent INR results and resulting warfarin doses.
- Details of all other medication.
- Specific details of any antiplatelet agents to be continued along with warfarin.
- Details of other diagnoses or risk factors relevant to anticoagulant therapy.

## Patients to be commenced on warfarin as an outpatient

Patients requiring elective initiation of warfarin (e.g. asymptomatic atrial fibrillation) can be referred to their local hospital Anticoagulant Clinic for this to be commenced as an outpatient. The standard GCAS Anticoagulant Monitoring and Clinic referral form can be used for this purpose (although details of inpatient anticoagulation will obviously be blank).

The same referral information (as above) is required. It is recommended that such patients do not start anticoagulant therapy in advance of their first anticoagulant clinic appointment.

## Return patients

Patients who were receiving warfarin prior to their current admission are often discharged in a less stable anticoagulant state and sometimes on a different warfarin dose. These patients will have an existing anticoagulant clinic appointment, however it may be appropriate to bring this forward. Therefore, prior to discharge, ward staff should ensure such patients have a suitable appointment (no longer than 2 weeks post discharge) with their usual anticoagulant clinic. Details of this modified appointment along with three most recent inpatient INR results and corresponding warfarin doses from their inpatient stay should be recorded in their yellow booklet.

# Reversal of Anticoagulant Therapy

## Introduction

Reversal of anticoagulant therapy may be necessary when a patient is found to be over-anticoagulated, develops bleeding problems or requires an invasive procedure. The general principles are similar in each situation and all cases require an individualised risk:benefit assessment. Management of surgery in patients receiving warfarin is covered in detail on page 88.

Patients with major or life-threatening bleeding, irrespective of their indication for anticoagulation (even patients with prosthetic metal heart valves) will usually require complete reversal of their anticoagulant therapy, at least temporarily.

Patients with minor bleeding, or over-anticoagulated without bleeding, will usually require temporary cessation of anticoagulant therapy (+/- small doses of reversing agents) to achieve a low-therapeutic level of anticoagulation.

## General management and drug therapy

### Heparin reversal

**Intravenous unfractionated heparin**

- Stop heparin.

  Heparin has a short elimination half-life of 30 - 90 minutes, although may be longer in renal failure.

- Protamine sulphate.

  This drug is ***only required in severe bleeding cases*** where there is likely to be a large amount of circulating heparin.

  Protamine sulphate (1mg) neutralises 100 units of heparin.

  **Administer protamine up to a maximum of 50 mg in a single dose as slow IV infusion over 10 minutes (anaphylaxis has been reported, see page 18 for Management of Anaphylaxis).**

  This drug should be avoided in patients with allergies to fish or fish products.

**Subcutaneous low molecular weight heparin (LMWH)**

- Stop LMWH.

  Most LMWHs have an elimination half-life of around 2 - 4 hours following subcutaneous injection, although this can be prolonged in renal failure.

- Protamine sulphate.

  The anticoagulant effects of LMWH are not completely reversed by protamine sulphate, but this drug should be considered if patients are suffering significant haemorrhage following recent (< 12 hours) administration of a therapeutic dose of LMWH.

  **Protamine doses are the same as for reversal of unfractionated heparin (1 mg of protamine per 1 mg of enoxaparin or 100 units of dalteparin or tinzaparin), but may need repeated as further LMWH is released from its subcutaneous depot.**

**Continues on next page**

## Oral warfarin reversal

**Life-threatening haemorrhage (e.g. intracranial, GI)**

All patients, including those with prosthetic heart valves, should have their anticoagulation completely reversed (aiming for normal PT and APTT) in the presence of life-threatening haemorrhage or trauma.

- Stop warfarin
- **Give Phytomenadione (Vitamin $K_1$) 5 mg IV (in 100 ml glucose 5% over 15 - 30 minutes).**
- **Give intravenous prothrombin complex concentrate (Beriplex®)**
  - **Dose according to table below. Maximum dose is 5000 units (200 ml).**
  - **Reconstitute 500 unit vial of Beriplex® to 20 ml using the sterile water and the reconstitution device supplied.**
  - **Infuse immediately at an infusion rate not exceeding 8 ml/minute.**
  - Contraindicated in patients with allergy to heparin, citrate or with suspected heparin induced thrombocytopenia, and use with extreme caution in patients with disseminated intravascular coagulation (DIC) or recent (< 1 month) venous thromboembolism, myocardial infarction or thombotic stroke.

**Table 1 – Beriplex® dose adjustment according to INR**

| INR | Approximate Dose |
|---|---|
| 2 - 3.9 | 1 ml/kg = 25 International units/Kg |
| 4 - 6 | 1.4 ml/kg = 35 International units/Kg |
| > 6 | 2 ml/kg = 50 International units/Kg |

Recheck coagulation status after 20 - 30 minutes and at 4 - 6 hours and 24 hours (or earlier if clinically indicated). Further doses of Phytomenadione (Vitamin $K_1$) may be required in cases of extreme overdose.

**Less severe haemorrhage (e.g. haematuria, epistaxis)**

- Stop warfarin for 1 - 2 days, and until INR has fallen to therapeutic levels and bleeding stopped.
- **Give phytomenadione (Vitamin $K_1$) 0.5 - 1 mg IV. Use insulin syringe to measure required volume before adding to 100 ml glucose 5% and infusing over 15 - 30 minutes.**

  **N.B. 0.5 mg = 0.05 ml. 1 mg = 0.1 ml.**
- Re-assess regularly.

**Continues on next page**

**General management and drug therapy continued**

**Asymptomatic INR > 8 or INR 5 - 8 and high bleeding risk (e.g. recent surgery)**

- Stop warfarin, monitor INR, and restart when INR < 5.0.
- Consider giving:

  **Phytomenadione (Vitamin $K_1$) 0.5 mg IV or 2 mg orally (use paediatric IV formulation orally).**
- Check INR next day.

**INR 5 - 8, asymptomatic**

- Stop warfarin, monitor INR and restart warfarin when INR < 5.

## Reversal of Antiplatelet Therapy

- Commonly used antiplatelet agents (including aspirin and clopidogrel) cause irreversible platelet inhibition, and therefore their effect may last up to 7 - 10 days following drug cessation.
- If a patient suffers life-threatening bleeding while being treated with combination antiplatelet agents (i.e. aspirin and clopidogrel) consideration should be given to treatment with platelet transfusion. *In vitro* evidence suggests that such dual antiplatelet therapy may be temporarily overcome by treatment with 2 - 3 adult doses of platelets.

## Reversal of new anticoagulant agents

Newer oral anticoagulant agents which are now available include:

- Dabigatran (Pradaxa®) – a direct Factor IIa (thrombin) inhibitor.
- Rivaroxaban (Xeralto®) – a direct Factor Xa inhibitor.
- Apixaban (Eliquis®) – a direct Factor Xa inhibitor.

These agents are not easily reversed, but fortunately they have relatively short half-lives (around 8 -12 hours). In renal impairment the half-life of dabigatran will be significantly prolonged, however the drug can be cleared by dialysis.

If patients receiving any of these new agents suffer major haemorrhage or require emergency surgery, then the following is recommended:

- Ascertain time of most recent dose of anticoagulant agent.
- Administer no further anticoagulant agent.
- Check coagulation screen (including PT, APTT and TCT) and renal function (U&Es).
- Discuss urgently with your local haematologist.
- Maintain cardiovascular status with fluid, red cell and blood product support as necessary (refer to Major Haemorrhage guideline, page 27).
- Consider possibility of delaying surgery until anticoagulant effect dissipated.

Further anticoagulant-specific advice can found on StaffNet, Clinical Guideline Electronic Resource Directory and search in the 'Haematology' section..

# Management Plan for Patients on Warfarin in the Peri-operative Period

## Introduction

This guideline aims to balance the competing risks – thrombosis versus haemorrhage – that anticoagulated patients face in the peri-operative period. In doubtful cases it is usually safer to omit anticoagulant drugs rather than over treat but each case needs individual assessment and you should consult senior colleagues and/or seek Haematology advice readily.

## Emergency admissions

In anticoagulated patients admitted with trauma, major bleeding or for emergency surgery the risks from haemorrhage generally far outweigh the thrombotic risks (even in high thrombotic risk patients).

*Full and immediate anticoagulation reversal is required –*

1. Check INR, full coagulation screen, full blood count and cross match blood.
2. Withhold warfarin
3. Reverse anticoagulation fully and rapidly (see page 85)
   - give **vitamin $K_1$ (phytomenadione) IV 5 mg as a single dose.**
   - give **Prothrombin Complex Concentrate (e.g. Beriplex®, 25 - 50 units/kg – maximum dose 5000 units)** according to the INR level.
4. Recheck full coagulation screen and full blood count.
5. If any concerns or uncertainty, discuss with on-call haematologist.
6. Proceed to surgery as appropriate.
7. **Only when you are sure** the risk of bleeding has abated, re-anticoagulate as appropriate to the patient's thrombotic risk category using the guideline for elective admissions (see below).

## Elective admissions - risk stratification

**Invasive procedures can be classified as to their risk from bleeding.**

**Low risk of bleeding:**

1. Standard dental procedures e.g. simple extractions $\leq$ 4 teeth
2. Routine upper GI endoscopy or colonoscopy including simple biopsy (unless part of the national bowel cancer screening programme – see below)
3. Cataract extraction and lens implantation

**High risk of bleeding:**

1. Any colonoscopy performed as part of the national bowel cancer screening programme, polypectomy, endoscopic treatment of varices, or ERCP
2. Most formal surgical procedures
3. Anaesthesia involving spinal or epidural anaesthetic

*Continues on next page*

**Extremely high risk of bleeding:**

1. Neurosurgical interventions

### Patients can be classified as to their risk from thrombosis.

**Low risk of thrombosis:**

1. Atrial fibrillation with normal heart valves and no previous embolism or stroke
2. Single episode of venous thromboembolism > 3 months previously
3. Sinus rhythm, tissue heart valve or modern (post-1990) metal aortic valve inserted > 2 months previously

**High risk of thrombosis:**

1. Atrial fibrillation with previous stroke, embolism, heart valve disease or any type of valve replacement
2. Metal mitral valve, any 'Ball and Cage' valve, pre-1990 metal aortic valve
3. Any artificial valve and previous embolism
4. Any heart valve placed within previous 2 months
5. Arterial embolism or venous thrombosis within previous 3 months
6. Prior recurrent venous thrombosis
7. Patient requiring target INR 3 - 4
8. Prior venous thrombosis and known high risk thrombophilia

## Elective admissions - management strategy

The general strategy for anticoagulant management is laid out in the following matrix.

**N.B.** Extremely high haemorrhagic risk procedures (e.g. neurosurgery) – consult the appropriate senior colleague and *do not apply this matrix*.

| | Low risk of thrombosis | High risk of thrombosis |
|---|---|---|
| **Low risk from bleeding** | ***In general continue warfarin therapy unchanged***<br>Proviso - INR should be checked < 48 hours prior to procedure;<br>It should not be supra-therapeutic and should be < 4 | |
| **High risk from bleeding** | **Target INR ≤ 1.4 for procedure**<br>1. Omit warfarin on day -5 (i.e. 5 days before surgery) – see next page<br>2. Give a prophylactic dose of **enoxaparin 40 mg SC daily at 1800 hours on each pre-operative inpatient day**<br>3. Restart anticoagulation post-operatively – see next page | **Target INR ≤ 1.4 for procedure**<br>1. Omit warfarin on day -5 (i.e. 5 days before surgery) – see next page<br>2. Use high dose heparin bridging therapy pre-operatively – see next page (LMWH) or page 91 (UFH*)<br>3. Restart anticoagulation post-operatively – see next page |

Some patients or procedures may not be easily classified into the above categories – if so, they should be discussed with the relevant senior clinician (e.g. haematologist, cardiologist, surgeon).

* UFH – Unfractionated heparin

## Elective admissions - stopping anticoagulation for surgery

**N.B.** Day zero is the day of the procedure, minus days are days prior to procedure, plus days are days after the procedure.

**1. Before surgery – at pre-assessment**

i. Ideally the patient should not be first on the operation list – this allows time for a day zero INR to be obtained prior to surgery if required.

ii. Day -7 (or earlier) measure INR.

iii. Day -5, stop warfarin: i.e. omit 5 doses prior to theatre.

iv. If high dose bridging therapy is appropriate follow the protocol below. Use low molecular weight heparin (LMWH) bridging as the method of choice where possible.

**2. High dose LMWH bridging in the pre-operative period**

Our aim is for patients to get this without hospital admission until day -1. Liaison between GP practice / district nurse team will usually be required. However, if a patient or carer is well motivated and safe disposal of sharps is assured then self-administration at home is possible.

i. Stop warfarin on day -5: i.e. omit 5 doses prior to theatre.

ii. Organise the prescription and administration of:

**enoxaparin SC 1.5 mg/kg on the afternoon of days -3 and -2** (i.e. between 1400 hours and 1800 hours) – see notes 1, 2 and 3 on page 92.

iii. Prescribe **enoxaparin SC 40 mg for 1800 hours** on day -1.

**3. Before surgery - on ward**

i. Patient should attend ward by 2 pm on day -1 for repeat INR.

ii. Obtain INR result that afternoon and if INR > 1.5 administer:

**vitamin $K_1$ (phytomenadione) IV 1 mg (0.1 ml) as a single dose.**

(Use an insulin syringe to draw up 0.1 ml before adding to 100 ml glucose 5% bag and administering over 15 - 30 minutes).

iii Recheck INR on day zero at 8 am.

## Elective admissions – restarting anticoagulation post-operatively

- *The first principle is do not prescribe any heparin or warfarin if there is evidence of active bleeding. If in doubt seek advice.*
- Ensure you have read all the accompanying notes prior to prescribing.
- Day zero is the day of the procedure, plus days are days after the procedure.

**Day 0 – All patients**

i. Give **enoxaparin SC 40mg at 1800 hours** (or 4 hours post-op, whichever is later) if no bleeding.

ii. Consider restarting warfarin. Restarting warfarin on day zero may be safe for some, as it will take several days to take affect. Never restart warfarin with an epidural catheter in situ.

*Continues on next page*

*Elective admissions – restarting anticoagulation post-operatively continued*

**Day + 1 and subsequent days – High thrombotic risk group**

Assess daily and consider:

i. Continued high risk of bleeding –

Give **enoxaparin SC 40 mg at 1800 hours**

ii. Low risk of bleeding and no epidural in place –

Give **enoxaparin SC 1.5 mg/kg at 1800 hours** + restart warfarin as soon as safe and practicable (i.e. adequate gut function).

iii. Low risk of bleeding and epidural in place –

Discuss with anaesthetist. Suggested dose:

**enoxaparin SC 1 mg/kg once daily at 1800 hours** (or alternatively **enoxaparin SC 40 mg once daily**) + do not restart warfarin until epidural catheter removed.

**Day + 1 and subsequent days - Low thrombotic risk group**

Assess daily and consider:

i. Continued high risk of bleeding –

Give **enoxaparin SC 40 mg at 1800 hours**

ii. Low risk of bleeding day +1 and +2 –

**enoxaparin SC 40 mg at 1800 hours** + restart warfarin as soon as safe and practicable (i.e. adequate gut function, no epidural in place).

iii. Low risk of bleeding day +3 onwards –

If there is no epidural in place increase dose to: **enoxaparin SC 1 mg/kg at 1800 hours.**

**All patients:**

Continue LMWH therapy until INR has returned to $\geq$ 2.

## Bridging therapy with unfractionated heparin in the peri-operative period

- *The first principle is do not prescribe any heparin or warfarin if there is evidence of active bleeding. If in doubt seek advice.*
- Use of unfractionated heparin (UFH) may occasionally be preferable to using LMWH e.g. when the ability to ensure rapid and complete reversal of heparin is required, where significant renal impairment exists or where standard monitoring of heparin effect is necessary.

1. On pre-operative day -1 commence UFH according to the schedule detailed in treatment of venous thromboembolism (VTE) (page 76).
2. Monitor APTT ratio and adjust UFH to achieve a result of 1.8 - 2.8.
3. Stop IV UFH 6 hours pre-operatively.
4. Recommence IV UFH 8 hours post-op (assuming haemostasis) at 50% of prior therapeutic dose.

   **N.B.** Do not give a loading dose post-operatively.
5. Assess APTT ratio on day +1 and **slowly** increase UFH dose to achieve a ratio of 1.8 - 2.8.

*Continues on next page*

6. Restart usual dose of warfarin as soon as it is safe and GI tract function is judged adequate. Do not restart warfarin with an epidural catheter in situ.
7. On day +2, monitor APTT ratio and slowly adjust UFH to achieve a ratio of 1.8 - 2.8.
8. Stop IV UFH 6 hours prior to removal of epidural catheters.
9. Continue UFH until INR is $\geq$ 2.

## Contraindications to heparin / high dose bridging therapy with LMWH

**Absolute contraindication –**

History of heparin allergy or heparin-induced thrombocytopenia (HIT), applies to UFH and LMWH.

**Relative contraindication –**

1. High bleeding risk (e.g. recent major bleed, stroke, neurosurgery, etc. in previous month)
2. Creatinine clearance < 30 ml/minute [or eGFR < 45 ml/minute/1.73m$^2$]. Use of LMWH heparin may be possible with suitable downward dosage adjustment, otherwise consider the use of UFH. See guideline on heparin dosing in renal impairment in the Haematology section of Clinical Guidelines Electronic Resource Directory on StaffNet.

## Surgery with spinal or epidural anaesthesia

1. Epidural or spinal anaesthesia should not be initiated or removed unless the INR is $\leq$ 1.4 and there is no appreciable heparin effect.
2. Avoid insertion or withdrawal of an epidural catheter within 12 hours of 40 mg enoxaparin or within 30 hours of a therapeutic (1 - 1.5 mg/kg) dose of LMWH.
3. Avoid heparin administration (SC or IV) for 4 hours after removal of an epidural.

## Essential Notes

1. Enoxaparin is available in single use syringes of 40, 60, 80, 100, 120 and 150 mg. Do not prescribe a dose that requires partial use of a syringe as this impairs accurate dosing. The dose should not exceed 1.5 mg/kg - round down to the nearest appropriately sized syringe. Aim for the use of one syringe but, rarely, in heavy patients two full syringes may be required. (Examples: patient weighing 70 kg and due dose of 1.5 mg/kg – prescribe 100 mg; patient weighing 120 kg and due dose of 1.5 mg/kg – prescribe 180 mg but this requires use of 2 syringes to deliver this dose.
2. The maximum daily dose by this protocol is 180 mg of enoxaparin. In heavy patients (> 120 kg) do not extend the dose past this value without seeking senior advice. Consider use of the available bariatric guideline in very heavy patients, but avoid twice daily dosing of enoxaparin if an epidural is in place (see guideline on dosing of heparin in patients at extremes of weight in Haematology section of Clinical Guidelines Electronic Resource Directory on StaffNet).
3. Attention should be given to renal function throughout the period of LMWH use. Doses of enoxaparin will need to be reduced if eGFR is < 30 ml/minute/1.73m$^2$.
4. Restart warfarin with the patient's usual daily dose. *Do not use a loading dose regimen – it is safer to go safe and slow with the reintroduction of warfarin*.
5. If exposure to unfractionated heparin (UFH) exceeds 4 days, monitor platelet count every 2 - 3 days from day 4 to 14, or until heparin is stopped. Be alert for evidence of HIT.
6. Patients with relatively recent (< 100 days) prior exposure to heparin can develop HIT within hours of re-exposure to the drug.

# Management of Suspected Acute Coronary Syndrome (ACS)

N.B. Some of the recommendations in this guideline have been recently revised. Please check: StaffNet, Clinical guideline electronic resource directory and search in Cardiovascular system for further information.

## Introduction

Chest pain is one of the most common presentations at A&E. There is a long list of differential diagnoses.

## Assessment / monitoring

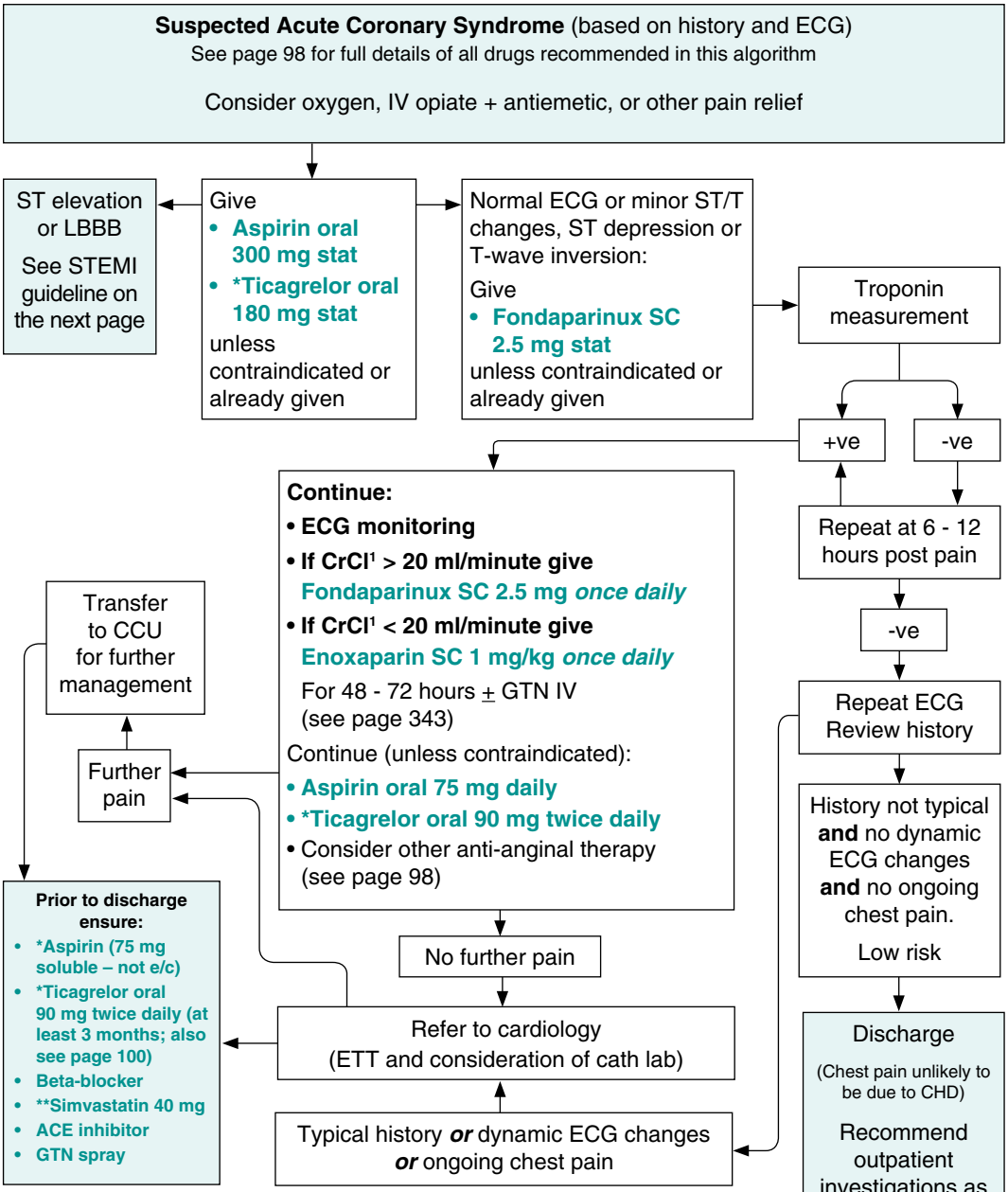
Record ECG (continuous monitoring), take a good history, measure blood pressure and perform all general assessment measures for an acute admission. Follow flow chart on the next page once ACS is established as the most likely cause of the presenting complaint.

Test for troponin if acute coronary syndrome is suspected with a suggestive history (even if no ECG changes) or there is another good clinical reason for testing. **Troponin testing should *not* be used as a catch-all test in a 'routine' battery**.

## STEMI

Primary percutaneous coronary intervention (PPCI) is the treatment of choice and most patients will be eligible. This is most effective when done as early as possible. ***Do not delay*** in making a decision about this – decisions will almost always be made in the ambulance or in A&E.

*Continues on next page*




* Ticagrelor – use with caution in patients with asthma / COPD / bradycardia. Check BNF, Appendix 1 for drug interactions before prescribing (ticagrelor is metabolised through Cytochrome P450-3A).
** Refer to secondary prevention of heart disease and stroke page 103.

[1] See equation on page 260

# Initial management of STEMI presenting to A&E

**Step 1**: Oxygen and monitor ECG.

**Step 2**: Call 999 and ask for "Emergency PCI Transfer".

**Step 3**: Commence medical treatment (see Box 1 page 96).

**Step 4**: Contact Golden Jubilee National Hospital (GJNH) 0791 761 6501 and give information of patient transfer.

**Step 5**: Fax ECG to GJNH if possible (fax 0141 951 5893)

If PPCI is not possible or there are logistical reasons causing a significant delay to PPCI, it may be necessary to administer thrombolytic therapy (see Box 2 on page 96).

Some patients with multiple co-morbidities may not be candidates for PPCI or thrombolysis.

## Contraindications to thrombolysis

### Absolute:

- Haemorrhagic stroke or stroke of unknown origin at any time
- Ischaemic stroke in preceding 6 months
- Central nervous system damage / neoplasms
- Major trauma / surgery / head injury within preceding 3 weeks
- Gastrointestinal bleeding within the last month
- Known bleeding disorder
- Aortic dissection

### Relative – discuss with senior staff before withholding:

- Transient ischaemic attack in preceding 6 months
- Oral anticoagulant therapy
- Pregnancy or within 1 month post partum
- Non-compressible punctures < 24 hours
- Traumatic resuscitation
- Refractory hypertension (systolic BP > 180 mmHg).
- Advanced liver disease
- Infective endocarditis
- Active peptic ulcer
- Terminal illness

*Continues on next page*

***If patient is for PPCI go to Box 1.***

***If patient is for Thrombolysis go to Box 2.***

**Box 1**

**Procedure for patients with STEMI who are eligible for PPCI**

Contact GJNH – see next page for contact details.

Prescribe and administer the following:

- **Morphine 5 - 10 mg by slow IV injection**
- **Metoclopramide IV 10 mg**
- **Soluble aspirin oral 300 mg immediately unless patient has already received a dose as per page 94 (75 mg if already taking aspirin regularly)**
- **Ticagrelor oral 180 mg stat**
- **Heparin IV 5000 units (unless patient has already received treatment dose of fondaparinux or enoxaparin)**

Consider prescribing the following, or if advised by the GJNH:

- **Glycoprotein IIb/IIIa inhibitor**
- **Metoprolol IV 5 - 15 mg or oral 50 - 100 mg if Killip Class 1 (withhold if heart rate < 65 bpm, systolic < 105 mmHg)**

**Box 2**

**Procedure for patients with STEMI who are for thrombolysis rather than PPCI**

Prescribe and administer tenecteplase in addition to all other drugs in box 1 (provided there are no contraindications), with the exception of the stat dose of ticagrelor, which should be substituted with **clopidogrel oral 300 mg stat**. Then prescribe **ticagrelor oral 90 mg twice daily** starting 24 hours after thrombolysis..

| **Tenecteplase single weight adjusted bolus over 10 seconds** | | | |
|---|---|---|---|
| **Weight** | **Weight imperial** | **Dose** | **Volume** |
| < 60 kg | < 9 st 6 lb | 30 mg | 6 ml |
| 60 - 69.9 kg | 9 st 6 lb - 11 st | 35 mg | 7 ml |
| 70 - 79.9 kg | 11 st 1 lb - 12 st 8 lb | 40 mg | 8 ml |
| 80 - 89.9 kg | 12 st 9 lb - 14 st 2 lb | 45 mg | 9 ml |
| > 90 kg | > 14 st 2 lb | 50 mg max dose | 10 ml |

**N.B. 90 minutes post thrombolysis** – if pain persists or a review of ECG shows a fall in ST elevation < 50% contact GJNH regarding rescue PCI for non-reperfusion.

| Interventional Cardiology Referral Pathway – West of Scotland Regional Heart and Lung Centre | | |
|---|---|---|
| **Elective Referrals** | **Urgent Referrals**<br>Bed to Bed Transfer<br>***Do not withhold low molecular weight heparin on day of referral*** | **Emergency / Immediate Referrals** |
| Electronic referral via SCI Gateway | **Electronic referral via SCI Gateway** | **Call 999 before contacting GJNH on:**<br>**0791 761 6501**<br>The same mobile number will be used 24 hours a day but will divert to CCU out of hours.<br>Discuss patient with Cardiology SpR on-call.<br>*Transfer patient by A&E ambulance to GJNH Cath Lab / cardiology HDU as directed.* |
| The referrals will be reviewed by a cardiologist and the Cardiology Clinical Scheduler. The patient will then be placed on the elective waiting list according to proposed procedure. | Arrange transfer of patient as directed by Clinical Scheduler. | |
| | Ensure all available information is sent with patient. | Ensure all available information is sent with patient. |

# Drugs for acute coronary syndrome / STEMI and secondary prevention of MI



**Antiplatelet drugs – Refer to antiplatelet guideline on page 100.**

## Beta-blockers

**Atenolol oral 25 - 50 mg twice daily**

Or if evidence of heart failure:

**Bisoprolol oral 1.25 - 10 mg daily or**

**Carvedilol oral 3.125 - 25 mg twice daily**

*Caution: Avoid beta-blockers in patients with a history of asthma or bronchospasm.*

Alternative options are:

- Cautious test dose with a short-acting beta-blocker such as metoprolol (which may be switched to an alternative beta-blocker if tolerated).
- A rate limiting calcium antagonist e.g. verapamil or diltiazem *instead of a beta-blocker.*

**Statins – Refer to cholesterol guideline on page 103**

## ACE inhibitors (ACEI)

**Ramipril oral 2.5 mg twice daily initially. Increase after 2 days to 5 mg twice daily if tolerated.**

**Lisinopril** – dose according to systolic blood pressure:

- *Systolic blood pressure over 120 mmHg* **– initially give lisinopril oral 5 mg, followed by a further 5 mg 24 hours later, then 10 mg after a further 24 hours. Continue with 10 mg once daily orally for 6 weeks (or continue if heart failure).**
- *Systolic blood pressure 100 - 120 mmHg* **– initially give lisinopril oral 2.5 mg once daily and increase to maintenance of 5 mg once daily orally.**

For ACEIs:

- Check U&Es before first prescription to exclude significant renal impairment.
- Check U&Es at one week following initiation and each up-titration to assess renal function.
- If renal function deteriorating (> 20% increase in creatinine or creatinine > 220 micromol/L), consider stopping ACEI and seek specialist advice.
- If ACEI not tolerated due to cough, substitute with an angiotensin II receptor blocker.
- **Avoid** potassium supplements / potassium sparing diuretics, if possible.

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**Calcium-channel blockers –** may be considered if indicated

**Amlodipine oral 5 - 10 mg daily.** This is the preferred calcium-channel blocker for patients on a beta-blocker

**or**

**Diltiazem oral 60 mg three times daily or 200 - 500 mg long-acting formulation once daily (e.g. Tildiem LA®)**. Always prescribe diltiazem by brand name. Never prescribe a rate limiting calcium-channel blocker together with a beta-blocker unless advised by a consultant.

**Nitrates –** may be considered if indicated

**Isosorbide mononitrate oral 10 - 40 mg twice daily (prescribe 8 am and 2 pm).**

Nitrate free period recommended (usually at night) to avoid developing tolerance.

# Secondary Prevention of Coronary Heart Disease and Stroke – Antiplatelet Guideline

The following patients should have antiplatelet therapy for life (unless they develop an indication for warfarin):

- CHD (angina, acute coronary syndrome, post-CABG)
- Thrombotic stroke or transient ischaemic attack (TIA). See separate guidance (page 124)
- Peripheral arterial disease (intermittent claudication or post-graft)

**Aspirin oral 75 mg daily (dispersible tablet)** is the agent of choice (but see separate guidance for stroke and TIA). Enteric coated aspirin does not reduce gastrointestinal (GI) symtoms. Only if aspirin is contraindicated or the side effects are intolerable (see page 102) should **clopidogrel oral 75 mg daily** be used instead.

Caution with all antiplatelets – ideally blood pressure should be under control (< 150/90 mmHg) prior to commencing any antiplatelet agent, and certainly systolic < 180 mmHg.

## Combination antiplatelet regimens

**Table 1 – Antiplatelet dual therapy regimens**

| Indication | Drug regimens and duration |
|---|---|
| **Thrombotic stroke (also see additional note on next page)** | |
| Stable thrombotic stroke or TIA | See Secondary Prevention of Stroke and TIA guideline page 124 |
| Carotid artery stent | Aspirin oral 75 mg daily indefinitely AND<br>Clopidogrel oral 75 mg daily for 4 weeks. |
| **ST elevation MI** | |
| Primary PCI drug-eluting stent | Aspirin oral 75 mg indefinitely AND ticagrelor oral 90 mg twice daily for 6 months |
| Primary PCI bare metal stent | Aspirin oral 75 mg indefinitely AND ticagrelor oral 90 mg twice daily for 3 months |
| Angiography only / Medical management | Aspirin oral 75 mg indefinitely AND ticagrelor oral 90 mg twice daily for 3 months |
| **Non – ST elevation MI** | |
| PCI with drug-eluting stent | Aspirin oral 75 mg indefinitely AND ticagrelor oral 90 mg twice daily for 6 months. |
| PCI with bare metal stent | Aspirin oral 75 mg indefinitely AND ticagrelor oral 90 mg twice daily for 3 months |
| Medical management | Aspirin oral 75 mg indefinitely AND ticagrelor oral 90 mg twice daily for 3 months |

Table continues on next page

| Table 1 – Antiplatelet dual therapy regimens (continued) | |
|---|---|
| **Indication Indication** | **Drug regimens and duration** |
| **Elective PCI in stable coronary artery disease** | |
| Drug-eluting stent | Aspirin oral 75 mg daily indefinitely AND<br>Clopidogrel oral 150 mg daily for 1 week, then 75 mg daily for 51 weeks |
| Bare metal stent | Aspirin oral 75 mg indefinitely AND<br>Clopidogrel oral 75 mg daily for 4 weeks.<br>Some patients may receive clopidogrel 150 mg daily for the first week and/or a 3 month course of clopidogrel at the discretion of the interventional cardiologist. |

**Notes**

- Coronary artery stents: Do not discontinue antiplatelet dual therapy sooner than the recommended durations in Table 1 without prior discussion with the patient's interventional cardiologist (details can be found on patient's clopidogrel card). If an invasive procedure is required, and cannot be delayed till end of clopidogrel prescription, consult patient's interventional cardiologist for individual action plan.
- If there is significant carotid stenosis following acute stroke or TIA, patient may be considered for combination aspirin and clopidogrel, at the discretion of a stroke consultant, whilst awaiting carotid surgery.

## Combination warfarin and antiplatelet agents

This combination is associated with a significantly higher major haemorrhage complication rate than either agent alone, without offering any proven benefit in reducing ischaemic or thromboembolic events (except in patients with metallic prosthetic heart valves).

### Patients on warfarin who develop an indication for an antiplatelet agent (e.g. thrombotic stroke, ACS)

***Low thrombosis risk patients*** (e.g. moderate risk atrial fibrillation (AF), deep vein thrombosis (DVT) > 3 months previously) who develop an indication for dual antiplatelet therapy (e.g. AF patient requiring coronary stent) should stop warfarin or receive triple therapy for as short a time as possible. Consideration should be given to the use of a bare metal stent.

***High thrombosis risk patients*** (e.g. high risk AF, recent venous thromboembolism) developing an ACS, require specialist advice and be considered for triple therapy.

### Patients on antiplatelet agents who develop an indication for warfarin therapy (e.g. AF, DVT)

In patients with stable vascular disease, on a single antiplatelet agent, this agent should be discontinued for the duration of warfarin therapy.

In patients with unstable vascular disease (e.g. recent ACS or stent) receiving dual antiplatelet therapy warfarin should be commenced cautiously with close monitoring and discontinuation of aspirin +/- ticagrelor / clopidogrel earlier than planned should be discussed with an interventional cardiologist.

It is accepted that some high thrombotic risk patients, with low inherent bleeding risk, may merit short-term triple therapy, however each case should be considered individually with a full risk:benefit assessment.

### Troponin positive ACS patients admitted on antiplatelet therapy

- On aspirin monotherapy – add **ticagrelor oral 90 mg twice daily** as per ACS protocol.
- On clopidogrel monotherapy due to aspirin gastrointestinal intolerance:
- - Switch to **aspirin oral 75 mg daily and ticagrelor oral 90 mg twice daily**
  - Add in proton pump inhibitor
- On clopidogrel monotherapy due to previous TIA / CVA:
- - Add **aspirin oral 75 mg daily**
  - Stop aspirin after dual antiplatelet therapy course is complete.
- On aspirin and clopidogrel after previous ACS admission – switch clopidogrel to **ticagrelor oral 90 mg twice daily**.

## Contraindications to aspirin

These are rare, but include aspirin allergy (aspirin-induced angioedema, asthma or skin rash).

***Relative contraindications for all antiplatelet agents (only prescribe on expert advice)*:**

- Recent gastrointestinal (GI) bleed
- Proven active peptic ulcer disease
- Breast feeding
- Haemophilia or other bleeding disorder

### GI symptoms and use of aspirin

- In patients with a history of bleeding peptic ulcer disease the combination of aspirin + proton pump inhibitor (PPI) **is safer than** clopidogrel alone (for secondary prevention).
- In patients developing GI symptoms after starting aspirin ***follow the algorithm below***.

**Patients developing GI symptoms after starting aspirin**

**Consider other contributory factors e.g.:**

- Excess alcohol intake
- NSAID use (these may be OTC and not prescribed)

↓

**If GI symptoms persist despite modification of contributory factors:**

Add treatment dose PPI (see page 49)

Enteric coated aspirin does not reduce GI symptoms – not recommended.

↓

**Patient complying and GI symptoms still persist?**

(This will be a rare event.)

↓

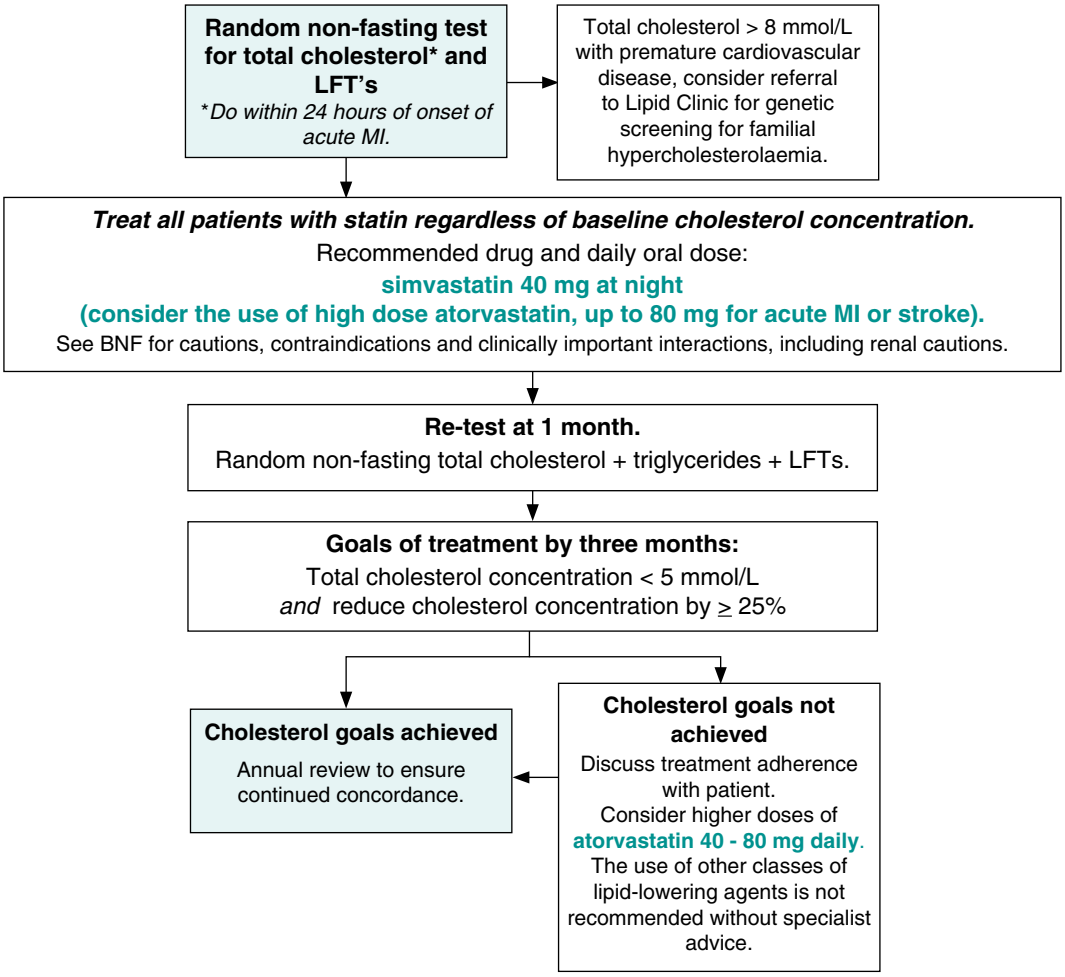
**Change to clopidogrel oral 75 mg daily** (***secondary prevention only***) **and stop PPI**.

Seek specialist gastroenterology advice if symptoms do not resolve.

# Secondary Prevention of Coronary Heart Disease and Stroke – Cholesterol Guideline

Patients with established vascular disease are at high risk and should be treated with a statin regardless of total blood cholesterol concentration i.e. previous MI / pre- or post-CABG / pre- or post-angioplasty / angina / angiographic coronary artery disease / ischaemic stroke or transient ischaemic attack / peripheral arterial disease / diabetic patients aged ≥ 40 years.

## Cholesterol Management Flowchart




*Continues on next page*

Atherosclerotic arterial disease is of multifactorial origin. No single risk factor, including cholesterol concentration, should be viewed in isolation.

- Encourage smoking cessation (consider nicotine replacement therapy – see Appendix 1).
- All other risk factors hypertension, diabetic control, should be addressed (see separate guidelines).
- **Aspirin oral dispersible 75 mg daily** (not enteric coated) should be taken by all those with occlusive arterial disease in the absence of contraindications (active peptic ulceration, a bleeding disorder or true hypersensitivity).
- Consider treatment with ACE inhibitors, especially in patients with left ventricular dysfunction or heart failure.
- Consider beta-blockers, and ensure attendance at a rehabilitation programme, for patients after myocardial infarction.
- Dietary and other lifestyle advice e.g. alcohol, obesity, physical activity, should be given.

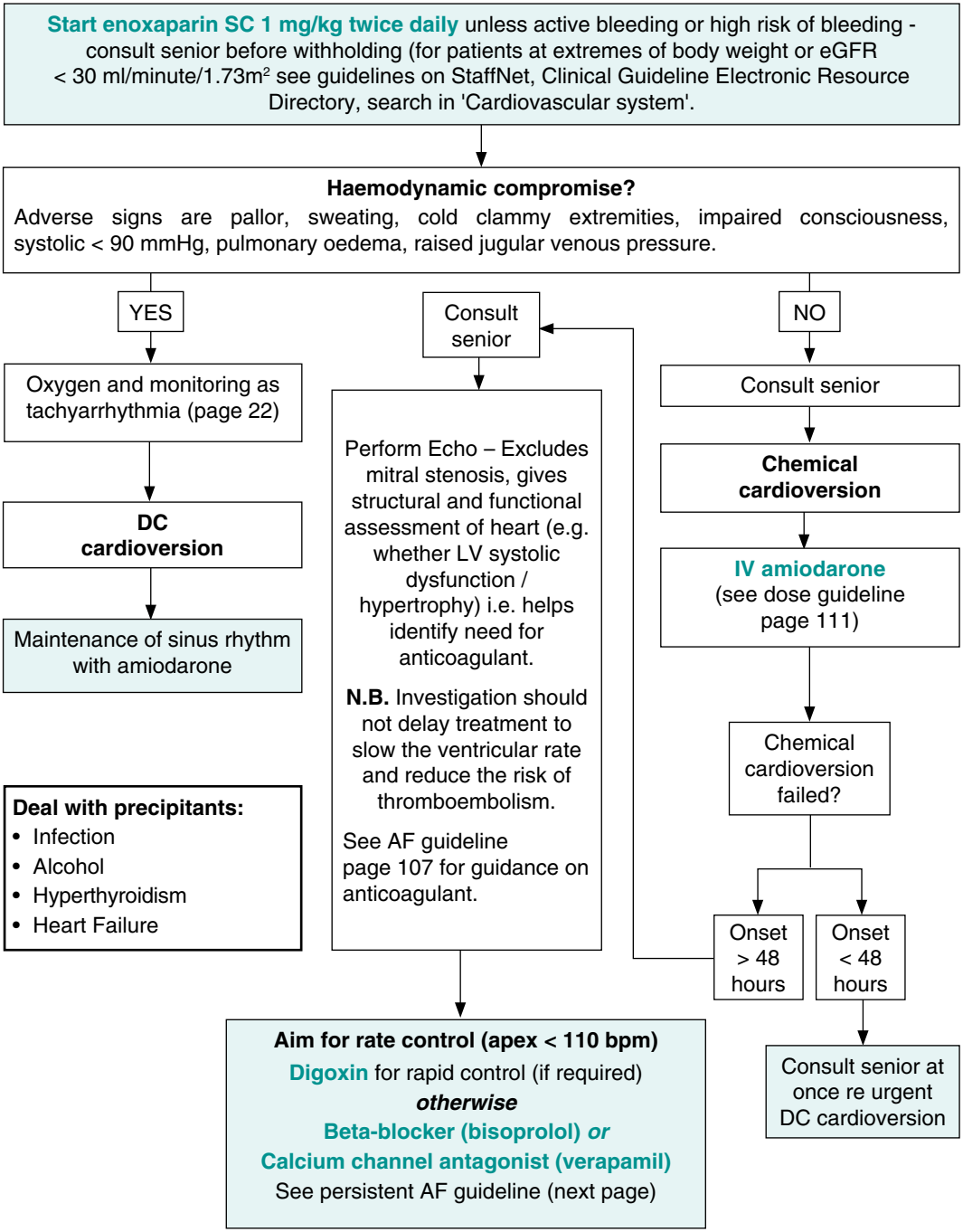
# Atrial Fibrillation (AF) or Flutter – Recent Onset

**Requiring admission, or onset during admission for other problem e.g. post-surgery.**

- Follow guidance for tachyarrhythmia (page 22).
- Haemodynamic compromise is an indication for rapid DC cardioversion - always use sedation or general anaesthesia.
- If the patient is haemodynamically stable, (no reduced conscious level, systolic BP > 90 mmHg, no chest pain and no heart failure), and onset < 48 hours, consider chemical cardioversion with IV amiodarone.
- Control ventricular rate with oral beta-blocker or rate-limiting calcium channel blocker (or digoxin IV if heart failure is present).
- If chemical cardioversion fails, consult senior medical staff re electrical cardioversion.
- Do echo and consider warfarin - see page 78 for dose initiation regimen.
- Remember – many cases of new onset AF or flutter will spontaneously revert to sinus rhythm – particularly if there is an obvious precipitating cause such as pneumonia, alcohol intoxication, hyperthyroidism or surgery.
- Cardioversion is much less successful in established AF or flutter than in new onset, and, if being considered, should not be delayed. Anticoagulant cover required if onset > 48 hours, so 4 - 6 week delay required.

*Continues on next page*

# Algorithm for Cardioversion of AF



# Atrial Fibrillation (AF) – Persistent

## Objectives

**Diagnostic:**

1. Exclude thyrotoxicosis.
2. Exclude acute (binge) or chronic alcohol consumption.
3. Exclude mitral stenosis and other valve problems, see below.
4. Determine if there are echocardiographic risk factors for stroke or thromboembolism.
5. Identify concomitant left ventricular (LV) systolic dysfunction and heart failure.

**Therapeutic:**

1. Relieve symptoms – often only rate control required; diuretic may also be needed (often only on temporary basis).
2. Target ventricular (apex or ECG) rate < 110 bpm. If still symptomatic, aim for lower rate, < 80 bpm.
3. Assess thromboembolic risk and anticoagulate as appropriate (see flow chart page 110).
4. In some cases, consider restoration of sinus rhythm by electrical or pharmacological cardioversion (only attempt chemical or electrical cardioversion after adequate anticoagulation with warfarin; risk of thromboembolism if not anticoagulated; limited long-term success).
5. Treat concomitant LV systolic dysfunction / heart failure.

## Essential investigations

1. A resting 12-lead ECG - confirms diagnosis, shows the ventricular rate, may indicate presence of structural heart disease.
2. Thyroid function tests.
3. Liver enzymes if alcohol abuse is suspected.
4. A transthoracic echocardiogram – excludes mitral stenosis, gives structural and functional assessment of heart (e.g. whether LV systolic dysfunction / hypertrophy) and therefore helps identify need for warfarin.

**N.B.** Investigation should not delay treatment to slow the ventricular rate and reduce the risk of thromboembolism.

## Ventricular rate control

1. Target ventricular (apex or ECG) rate < 110 bpm. If still symptomatic then aim for lower rate, < 80 bpm.
2. Patients **without** heart failure should be started on:
   - A beta-blocker – **start with atenolol oral 25 mg twice daily and titrate up to 50 mg twice daily if ventricular rate still > 100 bpm. In frail older people consider starting dose of atenolol oral 25 mg once daily**
     **or**
   - A rate-limiting calcium-channel blocker (CCB) i.e. verapamil or diltiazem (but avoid if LV systolic dysfunction).

     **Start with verapamil (slow release) oral 120 mg once daily and titrate up to 240 mg once daily if ventricular rate still > 110 bpm.**

**N.B.** Beta-blockers and rate-limiting CCBs must not be combined except under specialist supervision.

- Digoxin has a **limited** role as first-line treatment for ventricular rate control. It can be used in **combination** with beta-blocker / rate-limiting CCB when control of the ventricular rate is difficult.

3. Patients **with** heart failure should be started on digoxin and follow the NHSGGC heart failure guideline.

| | |
|---|---|
| **Heart failure / LV Systolic Dysfunction** | See NHSGGC guidelines, ACE inhibitors and beta-blockers are strongly recommended.<br>Beta-blockers must be initiated under direction of a hospital physician. Rate-limiting CCBs should be avoided. |

## Patients to refer for specialist assessment / consideration of cardioversion

- Young age (< 50 years)
- Reversible precipitating cause of AF (e.g. alcohol binge, thyrotoxicosis, pneumonia, recent surgery) and no major structural or functional heart disease.
- Difficulty with ventricular rate control
- Valve disease
- LV systolic dysfunction / heart failure
- AF causing symptomatic limitation despite rate-limiting treatment e.g. heart failure, excessive exertional breathlessness, undue fatigue.

*Continues on next page*

# Prevention of stroke / thromboembolism

- Patients with both recurrent paroxysmal AF and sustained AF have a high risk of thromboembolism, particularly stroke. Compared to subjects without AF the absolute risk of stroke is, on average, increased by about 4-fold and the risk of stroke is about 4% per annum.
- This risk is greatest in patients with certain risk factors (see flow diagram on next page).
- For primary prevention, the risk of thromboembolism can be reduced substantially (by 60 - 70%) with warfarin therapy (target INR 2 - 3). This equates to 20 - 30 fewer strokes at the expense of 6 - 8 serious bleeding episodes, per 1000 patient years of treatment.
- Patients with AF and a previous stroke or transient ischaemic attack (TIA) have an absolute risk of a further stroke of the order of 10 - 12% per annum and an absolute benefit of approximately 80 fewer strokes per 1000 patient years of treatment. **N.B.** Patient with a suspected stroke or TIA should first be referred for rapid specialist assessment – see page 117.
- Advanced age is not a contraindication to warfarin.
- In patients with 'lone' AF, i.e. AF in a structurally normal heart and no other risk factors for thromboembolic disease, no anti-thrombotic therapy or aspirin is recommended.

## Who should receive anticoagulant therapy

- Patients with clinical risk factors or echocardiographic risk factors (see flow diagram on next page).
- Patients without contraindications to anticoagulant therapy.

### Cautions / contraindications to anticoagulant therapy

- Absolute contraindications include: active bleeding, pregnancy, stroke < 14 days.
- Relative contraindications include: significant bleeding risk e.g. active peptic ulcer or recent head injury; bleeding in the last 6 months; previous cerebral haemorrhage.
- Cautions include: recurrent falls, or alcohol abuse.

### Cautions / contraindications to aspirin

- Aspirin allergy (rare)
- GI bleeding (< 6 months)
- Active proven peptic ulcer
- Systolic BP > 180 mmHg or diastolic BP > 110 mmHg (see Antiplatelet Guideline page 100)

### Initiation and monitoring of warfarin therapy

Urgent anticoagulation required – use Age-adjusted warfarin induction regimen on page 78.

Anticoagulation not urgent - consider a slower regime such as low-slow-start warfarin. Details available on Staffnet / Clinical Guideline Electronic Resource Directory. This regime involves 2 mg being given daily for 2 weeks with once weekly monitoring. Contact anticoagulation pharmacist if more information is required (see Appendix 6 under GCAS for contact details).

### Combined warfarin and antiplatelet therapy

Adding aspirin to warfarin therapy does not reduce the risk of stroke but substantially increases the risk of bleeding. After PCI, short-term combined double or triple therapy is used according to cardiologist advice.

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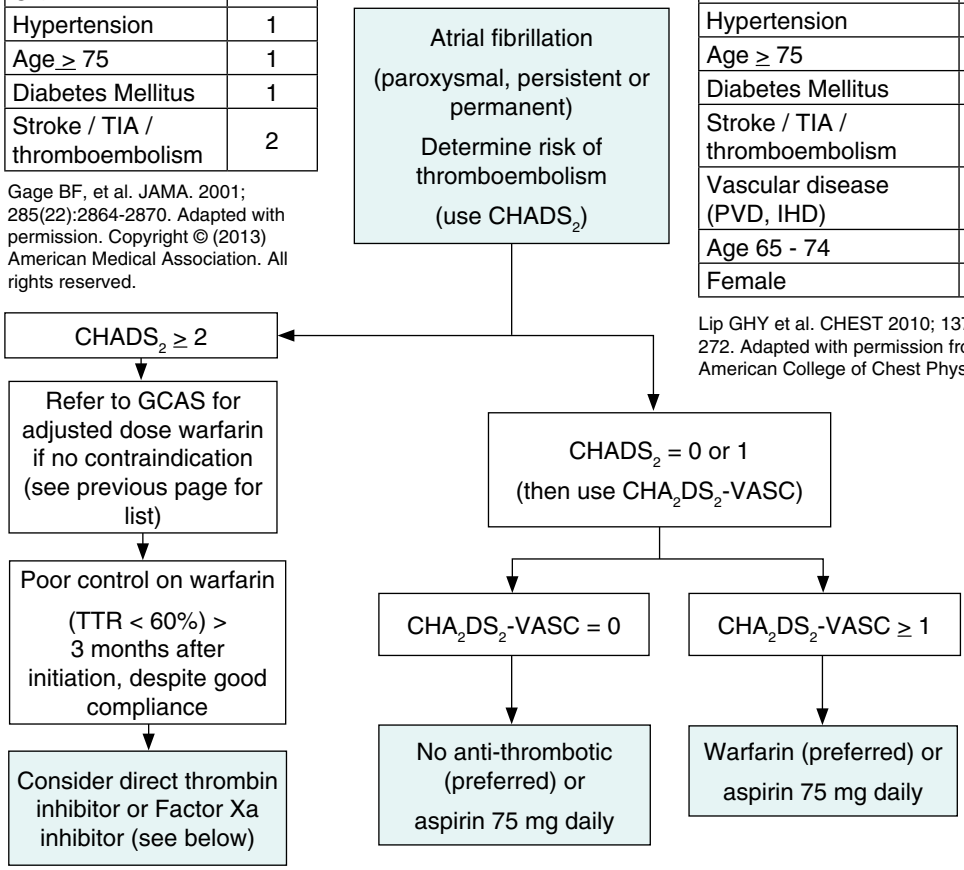
# Prevention of stroke / thromboembolism in AF

| $CHADS_2$ | Score |
|---|---|
| CHF | 1 |
| Hypertension | 1 |
| Age ≥ 75 | 1 |
| Diabetes Mellitus | 1 |
| Stroke / TIA / thromboembolism | 2 |

Gage BF, et al. JAMA. 2001; 285(22):2864-2870. Adapted with permission. Copyright © (2013) American Medical Association. All rights reserved.

| $CHA_2DS_2$-VASC | Score |
|---|---|
| CHF | 1 |
| Hypertension | 1 |
| Age ≥ 75 | 2 |
| Diabetes Mellitus | 1 |
| Stroke / TIA / thromboembolism | 2 |
| Vascular disease (PVD, IHD) | 1 |
| Age 65 - 74 | 1 |
| Female | 1 |

Lip GHY et al. CHEST 2010; 137(2): 263-272. Adapted with permission from the American College of Chest Physicians.




## New anticoagulants (direct thrombin and Factor Xa inhibitors)

- Warfarin is still the anticoagulant of choice
- New anticoagulants e.g. dabigatran and rivaroxaban, should only be considered in patients at high risk of stroke who are poorly controlled on warfarin (TTR < 60%), despite good compliance, at the recommendation of the GCAS (refer to GGC Adult Formulary for further restrictions). N.B. The new anticoagulants are only indicated as an alternative to warfarin in non-valvular atrial fibrillation patients, and should not be used as an alternative to warfarin in patients with prosthetic valves.
- Many contraindications to warfarin also apply to the newer agents.
- Dabigatran / rivaroxaban dosing guidance – see BNF for details. Do not use dabigatran if eGFR < 30 ml/minute/1.73m$^2$ whilst use rivaroxaban with caution and avoid if eGFR < 15 ml/minute/1.73m$^2$.

# Drugs for atrial fibrillation

See guidelines for management of persistent atrial fibrillation (page 107) and recent onset atrial fibrillation and flutter (page 105) for full details of the management of these conditions.

## Anticoagulation

On the recommendaton of GCAS, the choice of oral anticoagulant may change for selected patient groups.

**Warfarin – See page 109 for patients who should receive warfarin and page 78 for dosage advice.**

**Enoxaparin SC 1 mg/kg 12 hourly (unlicensed)**

## Chemical cardioversion

### Amiodarone

For chemical cardioversion (see guideline on recent onset atrial fibrillation and flutter on page 105).

**Amiodarone IV 300 mg infused over 1 hour *then* 900 mg over 24 hours through a central line or large peripheral line.**

**Amiodarone oral 200 mg three times daily for 1 week *then* 200 mg twice daily for 1 week *then* 200 mg daily. (Other oral regimens are sometimes used on the advice of a cardiologist.)**

**N.B.** Ideally, check baseline thyroid and liver function tests before starting. Interactions include digoxin and simvastatin (see BNF Appendix 1 for more details).

## Rate control

### Beta-blockers:

**Atenolol oral 25 - 50 mg twice daily**

**Bisoprolol oral 5 - 20 mg daily**

**Caution**: Avoid beta-blockers in patients with a history of asthma or bronchospasm. If there is no alternative, use atenolol or bisoprolol with extreme caution under specialist supervision.

**Continues on next page**

**Drugs for atrial fibrillation continued**

## Digoxin

**Loading dose – normal renal function**

**Digoxin oral (preferred route) 500 micrograms *followed 6 hours later by* 500 - 1000 micrograms in divided doses > 6 hours apart.**

**Digoxin IV 500 micrograms *followed 6 hours later by* 250 - 500 micrograms in divided doses 4 - 6 hours apart.**

**Loading dose – renal impairment**
(creatinine clearance < 30 ml/min)

**Digoxin oral (preferred route) 500 micrograms *followed 6 hours later by* 250 - 375 micrograms in divided doses > 6 hours apart.**

**Digoxin IV 250 - 500 micrograms**

**N.B.** Digoxin injection: 25 micrograms = 0.1 ml. Additional loading doses may be required; give according to ventricular (heart rate) response.

**Table 1 – Daily maintenance dose of digoxin**

| CrCl (page 260) | < 60 kg | | > 60 kg | |
|---|---|---|---|---|
| | Oral | IV | Oral | IV |
| > 50 ml/minute | **250 to 312.5 micrograms** | 175 to 200 micrograms | **250 to 375 micrograms** | 175 to 250 micrograms |
| 20 - 50 ml/minute | **125 to 187.5 micrograms** | 100 micrograms | **187.5 micrograms** | 125 micrograms |
| < 20 ml/minute | **62.5 to 125 micrograms** | 50 to 75 micrograms | **62.5 to 125 micrograms** | 50 to 75 micrograms |

**Target concentration range** 0.5 - 2 micrograms/L (6 - 24 hours after the dose)

**Time to steady state** 5 - 10 days

Concentration increased by amiodarone, diltiazem, quinine, verapamil (see BNF Appendix 1 for more details).

# Management of Acute Pulmonary Oedema / Heart Failure

## Introduction

Acute pulmonary oedema may be the first presentation of heart failure or an exacerbation of existing known heart failure. It also may be secondary to another cause e.g. atrial fibrillation (AF), other tachycardias or bradycardia, critical cardiac ischaemia, valvular disease or renal artery stenosis.

## Assessment

- If critical cardiac ischaemia / infarction, see thrombolysis / PCI guideline.
- Measure blood gases, record ECG and CXR and pulse oximetry.
- If in fast AF / flutter, see guideline page 105.

## General management / drug treatment

- Sit patient upright and give 100% oxygen via facemask unless $CO_2$ retention (see page 128 for interpretation of blood gases).
- Consider slow titrated small increments of intravenous diamorphine or morphine if associated chest pain or severe distress. Also consider antiemetic. Do not give opiate if patient is drowsy, exhausted or hypotensive. Give: **furosemide IV 50 mg (or in patients already receiving oral diuretics, give, intravenously, double the patient's normal oral dose). Repeat bolus at 30 mins to 1 hour. Double dose at first repeat. If further diuretic required - refer immediately to senior medical staff.**
- **Glyceryl trinitrate IV. Commence at 0.5 mg/hour. Titrate according to BP (but only if systolic BP $\geq$ 90 mmHg (see local dosing charts for details).**
- Consider CPAP (CPAP protocol on next page) or NIV if acidotic or poor response to furosemide and nitrates.
- Refer to senior medical staff and intensive care for consideration of intravenous inotropes or invasive ventilation.

**N.B.** Once the acute episode is resolved and the patient is more stable consider long-term management.

# CPAP in cardiogenic pulmonary oedema

- Continuous positive airway pressure (CPAP) can be considered in patients who have not responded to medical treatment. However, discuss this option with a senior.
- CPAP increases intrathoracic pressure, which reduces preload by decreasing venous return.
- CPAP lowers afterload by increasing the pressure gradient between the left ventricle and the extrathoracic arteries, which may contribute to the associated increase in stroke volume.
- Intubation should be considered in patients with persistent hypoxaemia on CPAP or persistent hypercapnia despite the administration of oxygen, morphine, diuretics, and vasodilators. In addition, intubation is required in the setting of apnoea or profound respiratory depression (respiratory rate < 10 bpm).

**Contraindications to CPAP:**

- Reduced conscious level (not responding to pain or unconscious on the AVPU scale: unable to protect airway therefore **consider invasive ventilation**)
- Dementia resulting in intolerance of therapy
- Systolic blood pressure < 90 mmHg
- Pneumothorax
- Facial trauma / base of skull fracture
- Type II respiratory failure / severe emphysema

**Complications of CPAP:**

- Hypotension – CPAP increases mean intrathoracic pressure, reducing systemic venous return and cardiac output
- Aspiration – gastric contents may be aspirated due to large volumes of air being blown into the stomach
- Gastric distension – large volumes of air swallowed can overcome resistance of lower oesophageal sphincter
- Anxiety – hypoxia and tight fitting mask can induce anxiety and panic

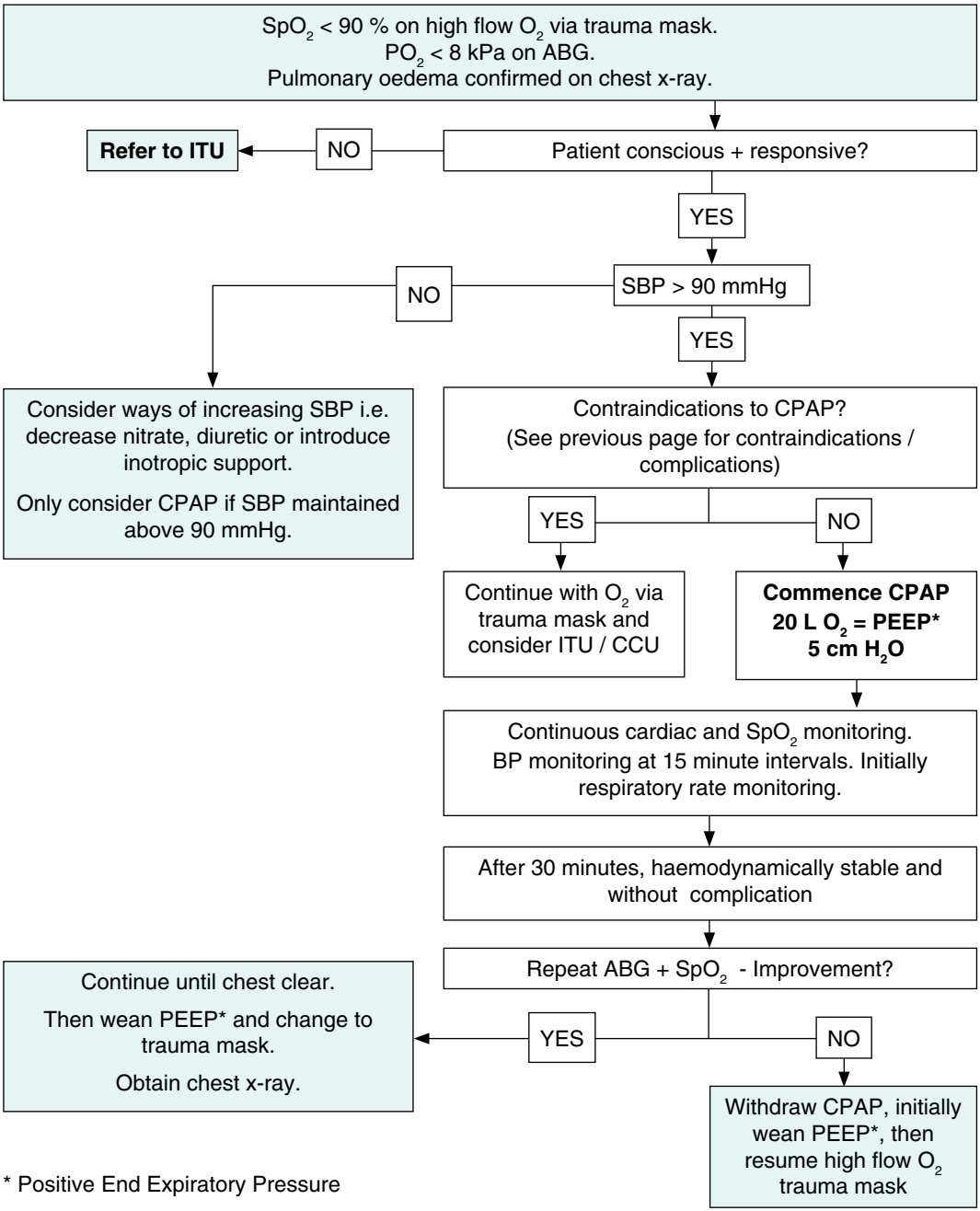
**When to stop CPAP:**

Continue CPAP until chest clear of rales and haemodynamically stable. Initially wean airway pressure then wean supplemental oxygen and change to standard facemask.

If there has been no clinical improvement after 30 minutes, CPAP should be stopped.

*Continues on next page*

## CPAP algorithm




* Positive End Expiratory Pressure

# Management of Hypertension

The full NHSGGC hypertension guideline is currently under review and once updated will be availableon StaffNet, Clinical Guideline Electronic Resource Directory and search in Cardiovascular system.

## Introduction

Hypertension is usually asymptomatic, often going unnoticed or untreated. It increases the risk of coronary heart disease (CHD), heart failure, stroke and renal disease. Only 25% of patients will achieve satisfactory control of blood pressure with one drug alone. Many will require drugs from 3 different groups. Compliance with medication is poor, as in many long-term conditions, but particularly when the condition is asymptomatic. Emergency or urgent situations regarding hypertension are rare, but when they present must be treated immediately.

### Hypertension emergencies

These include encephalopathy, aortic dissection, phaeochromocytoma, LVF with severe hypertension or eclampsia or recreational drug-induced severe hypertension which can lead to MI. These need rapid but not immediate or precipitous treatment. **Seek immediate on-call consultant advice.**

### Hypertension urgencies

These include severe hypertension with Grade 3 or 4 retinopathy and headache but no other features, which need around a 25% reduction over 6 hours or so. **Seek immediate on-call consultant advice.**

## General management

Most hypertension is managed well by GPs and that should be the default. It is part of the Quality and Outcomes Framework of the nGMS contract. Only when there is a problem in achieving targets after trying at least 3 drug groups in combination, unusual variability in blood pressure measurement, certain other co-morbidities such as AF or heart failure or an obvious cause of the hypertension (e.g. renal failure), is expert care required.

Non-drug treatment (management of obesity, moderating alcohol intake, reduction in salt intake, and increased exercise) should be instituted in all patients, where relevant. All other cardiovascular risk factors should be addressed e.g. smoking and diet.

Compliance issues require to be addressed.

It is important that return outpatient appointments are not offered unnecessarily and that outpatient recommendations for prescribing are in line with the agreed guidelines.

# Management of Acute Stroke 1

## Presentation with focal neurological symptoms, < 24 hours

### Introduction

The sudden onset of **focal** neurological symptoms implies a transient ischaemic attack (TIA) or stroke. A diagnostic distinction can sometimes be made between patients with suspected TIA or stroke. For management purposes, however, patients with the recent onset of focal neurological symptoms should be managed according to the continuing presence, or absence, of symptoms when assessed.

**Focal** symptoms include weakness of limb(s), facial weakness, and vision or speech disturbance.

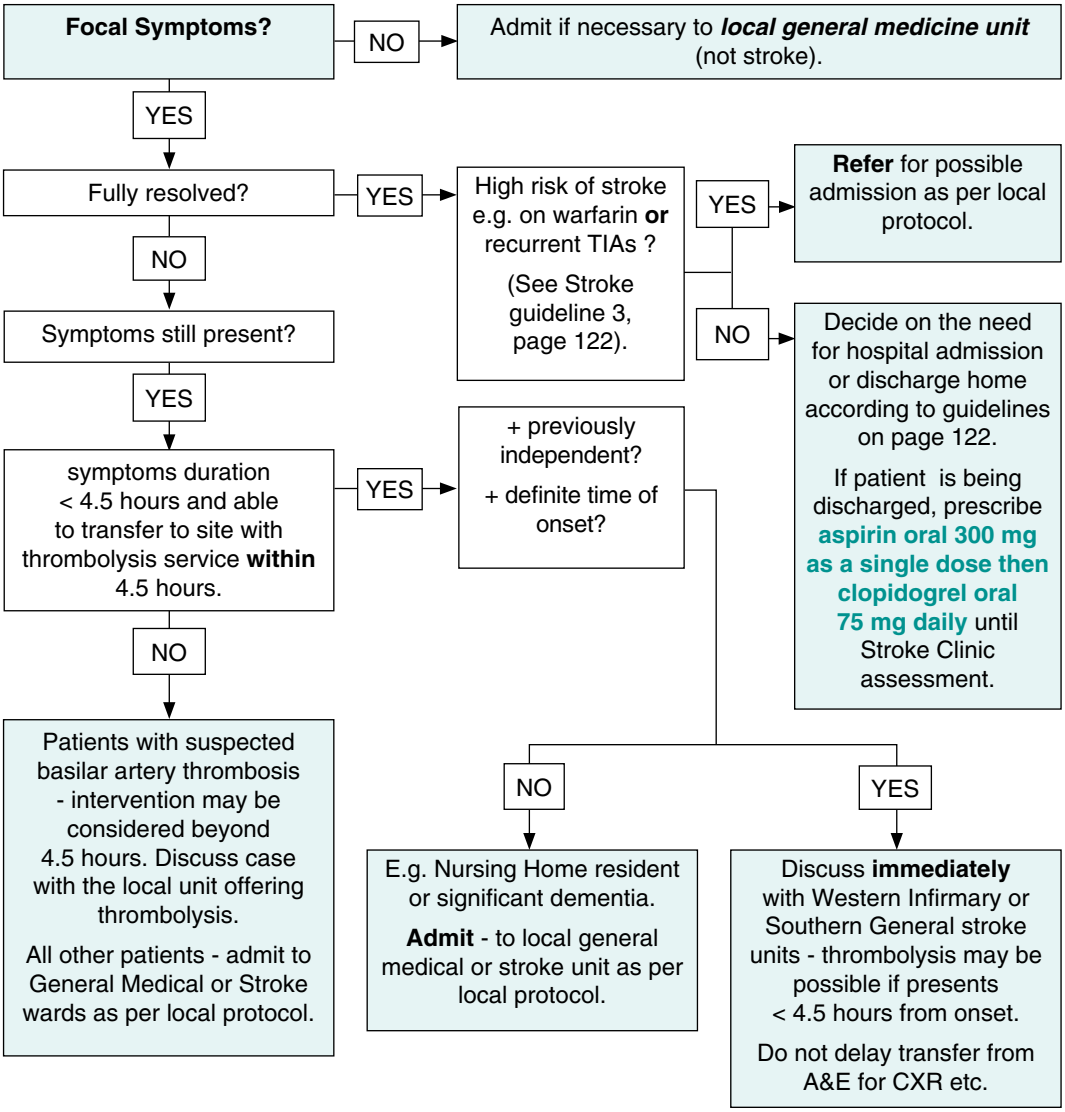
**Non-focal** symptoms include generalised collapse, loss of consciousness, and confusion without focal signs.

Stroke Unit care (available in all NHSGGC hospitals) offers advantages in terms of mortality and time to discharge home for all stroke patients. Selected patients, approximately 10% of all admissions, may achieve additional advantage with IV thrombolysis. However, this requires to be given in specialised stroke units within 4.5 hours of the onset of symptoms, or when last known to be definitely well. Therefore, refer immediately without delay to the appropriate Acute Stroke Unit – the Southern General hospital for hospitals south of the river Clyde and the Western Infirmary hospital for those north of the river.

See algorithm on next page which outlines the admission process of patients presenting with focal symptoms.

*Continues on next page*

# General management and drug therapy




TIA referral forms available in GP Practice and A&E Departments fax numbers on form.

# Management of Acute Stroke 2

## The first 24 hours

### Assessment / Monitoring

- Potential Thrombolysis case:
  - If the patient presents **within 4.5 hours of onset** of focal symptoms, thrombolysis referral may be appropriate – see Acute Stroke Guideline 1.
  - If patient presents > 4.5 hours, follow local protocol for stroke admissions.
- Request ECG, U&Es, glucose (non-fasting), LFTs, cholesterol, FBC and ESR
- Swallow test: check **before** prescribing and administering oral medication, oral fluids or diet.
- Check BP:
  - If < 100/60 mmHg seek cause and consider commencing IV fluids (see General management and drug therapy section on next page for details).
  - If > 200/130 mmHg seek evidence of malignant hypertension and consider treatment **only** after discussion with consultant.

    Otherwise, document blood pressure but **do not intervene**.
- Temperature: if > 37.5$^{O}$C look for evidence of infection and send blood / urine / sputum culture as appropriate and give paracetamol (orally or per rectum). If aspiration is probable, commence appropriate therapy (see General management and drug therapy on next page).
- Check oxygen saturation and treat hypoxaemia if necessary (see General management and drug therapy on next page).
- Withhold antiplatelet / antithrombotic medication until CT scan excludes haemorrhage.

CT brain scans should be requested as soon as possible after admission, and *immediate scanning should be carried out in the following instances:*

- Deteriorating consciousness level or coma.
- On anticoagulants (ensure INR / coagulation is checked and discuss with consultant whether reversal of anticoagulation is appropriate for patient).
- Brain stem symptoms plus bilateral limb signs or progression of signs or 'locked in'.
- Cerebellar stroke with headache or features of raised intracranial pressure.
- Severe headache.
- 'Stuttering' onset.
- Immunocompromised patients
- Unexplained fever
- Clinical signs of raised intracranial pressure

- Rhythm check – atrial fibrillation may be present (see page 105 for management).

*Continues on next page*

## General management and drug therapy

- **Do not prescribe** antihypertensive drugs, warfarin, heparin or steroids except after discussion with consultant.
- Blood glucose:
  - if low – correct
  - if high – may require insulin but important to avoid hypoglycaemia.
- All patients should receive fluids. Prescribe intravenous fluids as clinically indicated and adjust infusion volume of fluids as clinically necessary.
- Oxygen saturation: Target $O_2$ saturation is 95% – if less than 95% change posture, clear upper airway, start oxygen supplements as clinically appropriate and check arterial blood gases.
- **After CT brain**:

  If CT scan shows no haemorrhage prescribe a 'one-off' dose of:

  **aspirin oral 300 mg (or PR if swallow impaired).** Ensure aspirin is given immediately i.e. do not leave for administration at next morning's drug round.

  If patient has had thrombolysis, delay aspirin initiation for 24 hours. After the initial stat dose of aspirin, further antiplatelet therapy should be prescribed according to the NHSGGC Stroke Antiplatelet Guidelines (see StaffNet, Clinical Guidelines Electronic Resource Directory and search under 'Cardiovascular system'). If CT scan shows haemorrhage:

  - Consider Neurosurgical referral
  - Check urgent coagulation screen and discuss treatment of coagulopathies with consultant.
  - Stop all antithrombotics or anticoagulants patient may have been on previously, and consider anticoagulant reversal, see page 85 – should be discussed with consultant.

  If CT scan shows an alternative pathology (e.g. tumour, subdural haematoma), discuss with consultant.
- Temperature > 37.5°C and evidence of infection:

  If aspiration probable, commence appropriate antibiotic therapy while awaiting culture results (see Infections section) and

  **paracetamol (oral or per rectum) 1 g every four to six hours as required (maximum dose 4 g/day)**

  **N.B.** Consider dose reduction in patients with low body weight (≤ 50kg), renal / hepatic impairment or glutathione deficiency (chronic malnourishment, chronic alcoholism) to 15 mg/kg/dose up to four times daily (max 60mg/kg/day) An example is: paracetamol oral 500 mg four times daily.
- Atrial fibrillation: see page 105 for management.

**In the event of deterioration after admission, re-examine and specifically:**

- Check oxygenation and correct hypoxaemia with oxygen supplementation and postural change.
- Check blood pressure: treat as outlined at the start of this guideline.
- Check temperature: if pyrexial, check for signs of infection and treat. Also administer antipyretic (paracetamol dose as above).
- Check blood sugar and correct hypoglycaemia, consider insulin for hyperglycaemia (blood glucose > 9 mmol/L).
- Consider repeat ECG and treat as appropriate.

*Continues on next page*

- Reconsider potential indications for urgent CT or discuss repeat CT with stroke consultant.
- Proximal occlusion of the middle cerebral artery can lead to a large cerebral infarct which may go onto to develop cerebral oedema, causing raised intracranial pressure, deteriorating conscious level, loss of consciousness and eventual death. This syndrome is more common in younger stroke patients. If any clinical suspicion of Malignant Middle Artery Syndrome do immediate CT brain scanning and refer to Neurosurgery for possible hemi-craniectomy to relieve the intracranial pressure.

# Management of Acute Stroke 3

## Transient Ischaemic Attacks (TIAs)

### Guideline applicability

**N.B.** TIAs by definition have full resolution of all symptoms within 24 hours, but typically within minutes.

Patients with residual symptoms have had a stroke and should be managed according to Acute Stroke guidelines 1 and 2. If in any doubt, admit and follow Acute Stroke guideline 2.

### Suitability for discharge

Patients with TIA can be allowed home only in the following circumstances:

1. Fully conscious
2. Adequate communication
3. Safe swallow
4. Safe mobility (consider home environment)
5. Adequate social support
6. Clinic appointment requested and patient and family aware this has been done
7. Not on anticoagulants
8. No headache or confusion
9. No fluctuating symptoms
10. Must be single episode. Patients with recurrent TIAs should always be admitted.
11. Blood pressure > 100/60 mmHg and < 200/130 mmHg
12. Not in atrial fibrillation

*If in any doubt, admit and follow Acute Stroke Guideline 2: The First 24 hours.*

### Prior to discharge

If criteria 1 - 12 are all satisfactory, then discharge can go ahead but **only after** the following:

- Check, review and document in the notes:
  - Blood glucose
  - ECG
  - Blood pressure (admit if < 100/60 mmHg or > 200/130 mmHg).
  - FBC, U&Es, liver function and lipids.

*Continues on next page*

- Prescribe:

  **Aspirin oral 300 mg loading dose** then **clopidogrel oral 75 mg daily** in accordance with the NHSGGC Stroke Antiplatelet Guidelines (see StaffNet, Clinical Guidelines Electronic Resource Directory and search under 'Cardiovascular system').

- Advise patient not to drive (there is a 1 month ban after a TIA but DVLA do not need to be informed). Document in the notes the advice given.
- Advise patient and carers to return to A&E or call ambulance immediately if any further symptoms.
- Arrange outpatient TIA clinic review by contacting local TIA clinic – information available in A&E Departments. Complete the TIA referral form then phone (and fax) details to the Stroke / TIA secretary for your hospital.

# Secondary prevention of stroke and Transient Ischaemic Attack (TIA)

## Introduction

Secondary prevention of stroke should be considered in all patients as soon as possible after their stroke or TIA. Initiation of secondary prevention investigations and treatment should be guided by the stroke team, therefore, ensure that all **new** stroke or TIA patients are referred to the local stroke service.

## Drug therapy

### Antithrombotics

**Patients in sinus rhythm:**

First choice is:

**Clopidogrel oral 75 mg each day** (**N.B.** In TIA it would be an unlicensed indication).

If the patient is allergic or intolerant to clopidogrel then prescribe combination therapy:

**Aspirin oral 300 mg each day for 14 days or until hospital discharge, then reduce to aspirin oral 75 mg each day and**

**Dipyridamole MR oral 200 mg, starting with 200 mg each night and increasing to 200 mg twice daily if tolerated** (severe ischaemic heart disease is one possible contraindication).

**Patients in atrial fibrillation (AF):**

- Patients will usually start oral anticoagulants 10 to 14 days after the acute stroke but advice from a stroke consultant should be sought about this. Where patients are already on anticoagulation and have an ischaemic stroke, seek advice from a stroke consultant before resuming anticoagulation. Ensure stroke team advise before prescribing warfarin (see page 107 for information on AF management and page 78 for warfarin initiation information). If discharging patient home on warfarin ensure follow up arrangements are in place (see page 83 for referral to anticoagulation clinic).
- If contraindications to warfarin, seek advice from the stroke consultant.

**Patients with haemorrhagic stroke:**

- Antiplatelet drugs are contraindicated unless cause of intracerebral bleed resolves and patients also have concomitant ischaemic heart or stroke disease. This is a risk / benefit balance and advice should be sought from the stroke team.

*Continues on next page*

## Blood Pressure (BP)

After the acute phase, all patients with a BP > 130 mmHg systolic or > 80 mmHg diastolic should be considered for a:

- Long-acting angiotensin-converting enzyme inhibitor (ACEI) and a diuretic (such as bendroflumethiazide), if tolerated and not contraindicated.
- Add additional antihypertensives if BP remains above target level (see NHSGGC Hypertension Guideline). Even 'normotensive' patients (< 130 mmHg systolic or < 80 mmHg diastolic) may benefit from antihypertensive treatment, especially with ACEIs.

## Cholesterol

Unless contraindicated, treat all patients who have had an ischaemic stroke with a statin regardless of baseline cholesterol concentration. Recommended drug of choice is:

**Simvastatin oral 40 mg each night** (refer to NHSGGC Lipid Lowering Guideline on StafffNet).

## Diabetes

If initial blood sugar is elevated, investigate for diabetes including checking fasting blood sugar and haemoglobin A1c. If already diabetic, check HbA1c and aim for good control. This may be difficult to achieve for many patients, but this is an important, modifiable risk factor.

## Carotid disease

All stroke or TIA patients with symptoms potentially related to their carotid artery circulation territory should have carotid imaging requested immediately and the results discussed with the Stroke Consultant. No carotid investigation is required for patients with primary intracerebral haemorrhage.

In a patient with moderate to severe (> 50% stenosis) carotid disease, discuss immediately with the local Stroke Team to access suitability for surgery and the need for any alteration in secondary prevention medication.

## Cardiac disease

All stroke or TIA patients who do not have already known atrial fibrillation (AF) should be investigated for possible AF with a request made for either 48 hour or 72 hour ambulatory ECG monitoring (local protocols vary with availability). Echocardiography is used in selected patients e.g. with multiple cerebrovascular events or with otherwise unexplained stroke but the decision to request echo usually will be made by the stroke consultants.

## Health Promotion

- Smoking – Record tobacco consumption, advise smoking cessation and offer referral to Smoking Cessation Service (see Appendix 1).
- Exercise – Provide general supportive advice for healthy active lifestyle within functional limits.
- Weight – Record height and weight. Aim for improved BMI (Gold standard is < 25).
- Nutrition – Offer supportive advice for healthy eating, particularly for patients with diabetes or high cholesterol.
- Driving – Offer advice as per DVLA guidance – driving is prohibited for 1 month after event and longer if recurrent events or presence of a disability impairing driving, or if PSV/HGV driver.
- Alcohol – Advise on safe limits and refer to Addiction Team if appropriate.

Section 5

# Respiratory System

# Guidelines for Blood Gas Analysis

## Oxygen therapy

In critical illness, initial oxygen therapy is a reservoir mask at 15 L/minute.

For most acutely unwell patients, oxygen should be prescribed to achieve a target oxygen saturation of 94 - 98%.

For patients at risk of hypercapnic respiratory failure (e.g. exacerbation of chronic obstructive pulmonary disease (COPD), chest wall deformity, neuromuscular disorder, obesity-hypoventilation syndrome), oxygen should be prescribed to achieve a target oxygen saturation of 88 - 92%.

It is recommended that oxygen be commenced at 28% via a venturi mask pre-hospital and 24% via a venturi mask in hospital for patients with prior hypercapnic failure (i.e. required non-invasive ventilation - NIV).

For patients with COPD, nebulisers should be driven using an air cylinder and oxygen supplement via nasal cannulae. For patients with asthma or other conditions, nebulisers should be oxygen-driven.

Arterial blood gases should be rechecked 30 - 60 minutes after initiation of controlled oxygen or initiation of NIV, or immediately if clinical deterioration.

Oxygen is a drug and should be prescribed on the drug chart detailing delivery device, flow rate and oxygen concentration.

## Indications for blood gas analysis

- All critically ill patients.
- Unexpected or inappropriate hypoxaemia ($SpO_2$ < 94% in patients breathing room air or oxygen) or any patient requiring oxygen to achieve the above target range. Allowance should be made for transient dips in saturation to 90% or less in normal subjects during sleep.
- Deteriorating oxygen saturation or increasing breathlessness in a patient with previously stable hypoxaemia (e.g. severe COPD).
- Any previously stable patient who deteriorates and requires a significantly increased FiO2 to maintain a constant oxygen saturation.
- Any patient with risk factors for hypercapnic respiratory failure who develops acute breathlessness, deteriorating oxygen saturation, drowsiness or other symptoms of carbon dioxide retention e.g. COPD or neuromuscular disorders.
- Acutely breathless or with poor peripheral circulation in whom a reliable oximetry signal cannot be obtained.
- Severe metabolic disturbance e.g. diabetic ketoacidosis (DKA) or renal failure, hypothermia (temperature < 32°C), severe sepsis, shock or altered conscious level.
- Any other evidence from the patient's medical condition that would indicate that blood gas results would be useful in the patient's management (e.g. an unexpected change in the MEWS score or an unexpected fall in oxygen saturation of 3% or more, even if within the target range).
- Smoke inhalation / carbon monoxide poisoning / cyanide poisoning.

# Interpretation of blood gases

First consider oxygen and carbon dioxide; *patients die of hypoxia faster than any other blood gas abnormality.*

## 1. Examine the $PaO_2$ (normal range on air 10 - 13 kPa)

**Is the patient hypoxaemic?**

- If the $PaO_2$ is low, consider increasing the oxygen.
- If the $PaO_2$ is low in the context of chronic respiratory disease, consider what the normal level of $PaO_2$ would be for any given patient and aim for that.

  **Example**: *In some patients with COPD, simply targeting a $pO_2$ > 8 kPa (or oxygen saturations between 88 - 92%) will suffice, and will reduce the likelihood of $CO_2$ retention.*

**Is the $PaO_2$ normal?**

- Consider whether this is appropriate in the context of flow of oxygen delivered.

  **Example**: *If a 20 year old is requiring 60% oxygen via a venturi mask to maintain their $PaO_2$ in the normal range, then their oxygen delivery is significantly compromised.*

- **Rule of thumb**: % $O_2$ delivered **minus** (10 to 15) ⟷ expected $pO_2$

  **Examples**: 60% $O_2$ delivered **minus** (10 to 15) ⟷ then expected $pO_2$ 45 - 50 kPa

  28% $O_2$ delivered **minus** (10 to 15) ⟷ then expected $pO_2$ 13 to 18 kPa

## 2. Examine the $PaCO_2$ (normal range 4.6 - 6 kPa)

**Is the patient hypercapnic?**

- Do they have underlying COPD?

  *If so, give controlled oxygen using a venturi mask, targeting oxygen saturations of 88 - 92%, and optimise medical management. If unable to maintain oxygen saturations at this level or worsening hypercapnia / acidosis despite optimum therapy then discuss with ITU / consider non-invasive ventilation.*

- Are they tiring?

  *Patients who have had persistently increased work of breathing can begin to retain $CO_2$ and should be discussed with ITU.*

- Is their respiratory function suppressed?

  *Check patients have not been taking opiates or sedatives.*

- Patients with acute severe asthma who have a normal or raised $pCO_2$ merit early discussion with ITU.

**Is the patient hypocapnic?**

- If the patient is acidotic or has a normal hydrogen ion, then this is likely respiratory compensation for a metabolic acidosis.
- If the patient is alkalotic, then this is commonly due to hyperventilation.
- If the patient has a normal $PaO_2$, then they may have an underlying oxygen delivery problem e.g. pulmonary embolism.

Next consider acid-base balance.

### 3. Examine the hydrogen ion ($H^+$ normal range 35 - 45 nmol/L)

**If the $H^+$ is increased, the patient is acidotic**

- If the $PaCO_2$ is increased this is a respiratory acidosis

  *Common causes of respiratory acidosis include some exacerbations of COPD, respiratory depression e.g. opiate / sedative use or neuromuscular disorders*

- If the $PaCO_2$ is normal or reduced, this is a metabolic acidosis

  *Common causes of a metabolic acidosis include diabetic ketoacidosis (DKA), lactic acidosis, renal failure, drugs.*

**If the $H^+$ is reduced, the patient is alkalotic**

- If the $PaCO_2$ is reduced this is a respiratory alkalosis

  *Common cause of respiratory alkalosis includes hyperventilation.*

- If the $PaCO_2$ is normal or increased this is a metabolic alkalosis.

  *Common causes of a metabolic alkalosis include vomiting and diarrhoea.*

**If the $H^+$ is normal, then the patient may have a compensated acid-base disturbance**

- If the bicarbonate (normal range 22 - 27 mmol/L) is raised, then the patient has a compensated respiratory acidosis (commonly in severe COPD or neuromuscular disease).
- In DKA, the treatment should be adjusted according to the bicarbonate as it lags behind the hydrogen ion which normalises first (see DKA management page 276).

Venous gases can be used for following improvement in metabolic acidosis e.g. in DKA or for quick initial review of electrolytes in emergency situation.

# Guidelines on Oxygen and Oximetry

Guidelines on Blood Gas Analysis on page 128.

## Pneumonia

- In severe pneumonia use continuous monitoring.
- Adjust oxygen treatment to maintain target saturation as per page 149.
- Check arterial gases initially, and again if saturation falls.
- Consider referral to ITU if saturation cannot be maintained > 90%.

## Asthma

- Use continuous monitoring for persistent severe asthma (aim for saturation as per pages 132 and 134).
- Arterial gas measurement to exclude $CO_2$ retention if any clinical deterioration.

## COPD

See section on COPD, page 136.

## Shocked patient

- Oximetry may be unreliable due to poor perfusion.
- Patients should be given medium flow, high concentration oxygen via reservoir mask until condition assessed.
- Always check arterial gases as a baseline.

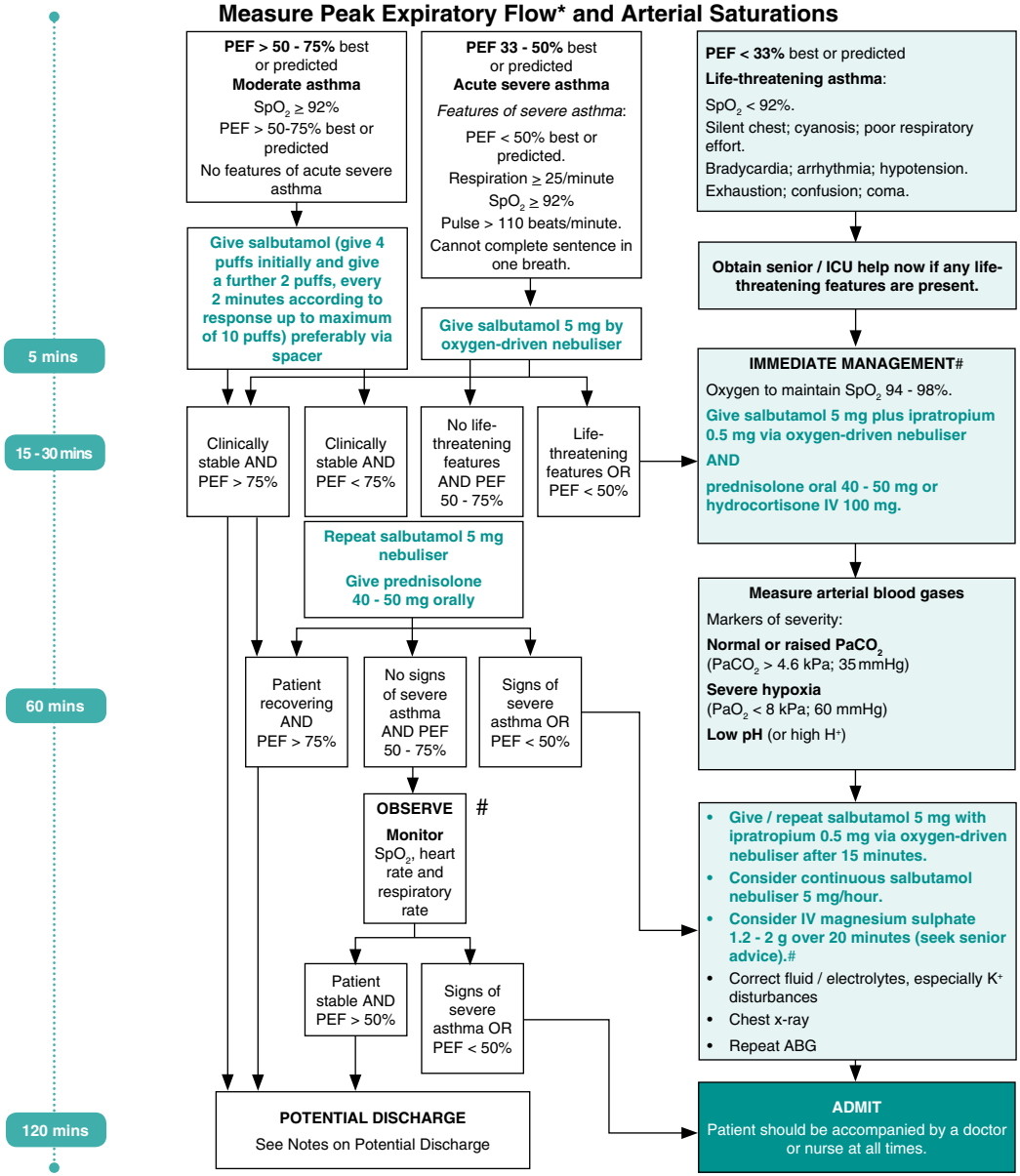
**N.B.** Do not rely on oxygen saturation alone in isolation from arterial gas measurement and/or clinical assessment.

# Chronic oxygen therapy

Oxygen in the home is provided to correct chronic hypoxia particularly if associated with cor pulmonale, and sometimes for symptomatic relief in intermittent hypoxia. Do not assess patients for home oxygen therapy during an acute admission but refer to your local respiratory department for review.

# Management of Acute Severe Asthma in Adults in A&E

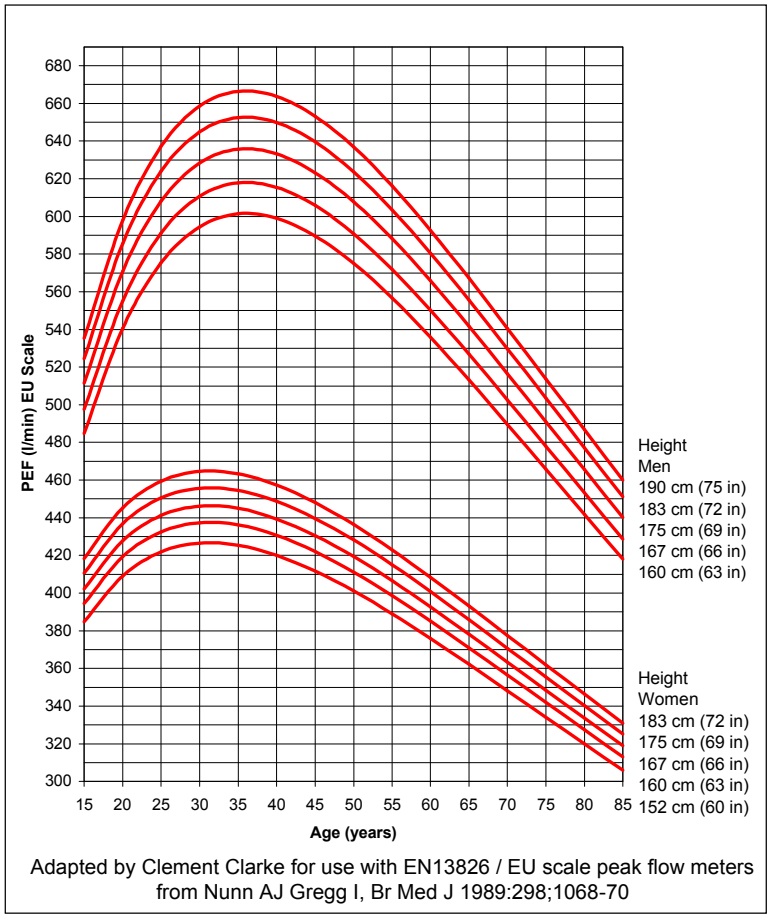
Scottish Intercollegiate Guidelines Network (SIGN). British Guidelines on the Management of Asthma. Edinburgh: SIGN; revised Jan 2012. (no. 101). Available from www.sign.ac.uk. Algorithm adapted with permission from the British Thoracic Society (# denotes minor changes).



## Notes on Potential Discharge from A&E #

- In all patients who received nebulised $Beta_2$ agonists prior to presentation, consider an extended observation period prior to discharge.
- If PEF < 50% on presentation, prescribe **prednisolone oral 40 - 50 mg/day for 5 days.**
- In all patients ensure treatment supply of inhaled steroid and $Beta_2$ agonist and check inhaler technique.
- Arrange GP follow up for 2 days post discharge.
- Fax discharge letter to GP.
- Refer to asthma liaison nurse / chest clinic.

## *Peak Expiratory Flow Rate – Normal Values




Adapted by Clement Clarke for use with EN13826 / EU scale peak flow meters
from Nunn AJ Gregg I, Br Med J 1989:298;1068-70

From SIGN Guideline 101 with permission

# Management of Acute Severe Asthma in Adults in Hospital

Scottish Intercollegiate Guidelines Network (SIGN). British Guidelines on the Management of Asthma. Edinburgh: SIGN; revised Jan 2012. (no. 101). Available from www.sign.ac.uk. Algorithm adapted with permission from the British Thoracic Society (# denotes minor changes).



**Features of acute severe asthma:**

- Peak expiratory flow (PEF) 33 - 50% of best (use % predicted if recent best unknown).
- Can't complete sentences in one breath.
- Respiration ≥ 25 breaths/minute.
- Pulse ≥ 110 beats/minute.

**Life-threatening features:**

- PEF < 33% of best or predicted.
- $SpO_2$ < 92%
- Silent chest, cyanosis, or feeble respiratory effort.
- Bradycardia, dysrhythmia, or hypotension. #
- Exhaustion, confusion, or coma. #

**If patient has any life-threatening feature:**

Measure arterial blood gases. No other investigations are needed for immediate management.

**Blood gas markers of a life-threatening attack:**

- Normal (4.6 - 6 kPa, 35 - 45 mmHg) $PaCO_2$
- Severe hypoxia: $PaO_2$ < 8 kPa (60 mmHg) irrespective of treatment with oxygen.
- A low pH (or high $H^+$).

**Caution:** *Patients with severe or life-threatening attacks may not be distressed and may not have all these abnormalities. The presence of any should alert the doctor.*

**Near fatal asthma:**

- Raised $PaCO_2$
- Requiring IPPV with raised inflation pressures. #

## IMMEDIATE MANAGEMENT

- Oxygen to maintain $SpO_2$ 94 - 98%.
  ($CO_2$ retention is not usually aggravated by oxygen therapy in asthma). #
- **Salbutamol 5 mg or terbutaline 10 mg via an oxygen-driven nebuliser.**
- **Ipratropium bromide 0.5 mg via an oxygen-driven nebuliser.**
- **Prednisolone oral 40 - 50 mg or hydrocortisone IV 100 mg or both if very ill. #**
- No sedatives of any kind.
- Chest radiograph only if pneumothorax or consolidation are suspected or patient requires IPPV. #

**If life-threatening features are present:**

- Discuss with senior clinician and ICU team.
- **Add IV magnesium sulphate 1.2 - 2 g infusion over 20 minutes (unless already given).**
- **Give nebulised $Beta_2$ agonist more frequently e.g. salbutamol 5 mg up to every 15 - 30 minutes or 10 mg continuously hourly. #**

## SUBSEQUENT MANAGEMENT

**If patient is improving continue:**

- Oxygen to maintain $SpO_2$ 94 - 98%.
- **Prednisolone oral 40 - 50 mg each day or hydrocortisone IV 100 mg 6 hourly.**
- **Nebulised $Beta_2$ agonist and ipratropium 4 - 6 hourly.**

**If patient not improving after 15 - 30 minutes:**

- Continue oxygen and steroids.
- **Give nebulised $Beta_2$ agonist more frequently e.g. salbutamol 5 mg up to every 15 - 30 minutes #**
- **Continue ipratropium 0.5 mg 4 - 6 hourly until patient is improving.**

**If patient is still not improving:**

- Discuss patient with senior clinician and ICU team.
- **IV magnesium sulphate 1.2 - 2 g over 20 minutes (unless already given). #**
- **Senior clinician may consider use of IV Salbutamol* or IV aminophylline or progression to IPPV. #**

Continues on next page

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## MONITORING

- Repeat measurement of PEF 15 - 30 minutes after starting treatment.
- Oximetry: maintain $SpO_2$ 94-98%.
- Repeat blood gas measurements within 1 hour of starting treatment if:
  - initial $PaO_2$ < 8 kPa (60 mmHg) unless subsequent $SpO_2$ > 92%
  - $PaCO_2$ normal or raised
  - patient deteriorates.
- Chart PEF before and after giving $Beta_2$ agonists and at least 4 times daily during hospital stay.

*Transfer to ICU accompanied by doctor prepared to intubate if:*

- Deteriorating PEF, worsening or persisting hypoxia, or hypercapnea.
- Exhaustion, feeble respirations, confusion or drowsiness. #
- Coma or respiratory arrest. #

## DISCHARGE

When discharged from hospital, patients should have:

- Been on discharge medication for 24 hours and *have had inhaler technique checked and recorded.*
- PEF > 75% of best or predicted and PEF diurnal variability < 25% *unless discharge is agreed with respiratory physician.*
- Treatment with **oral and inhaled steroids** in addition to bronchodilators.
- Own PEF meter and written asthma action plan.
- GP follow up arranged *within 2 working days.*
- Follow up appointment in respiratory clinic *within 4 weeks.*

Patients with severe asthma (*indicated by need for admission*) and adverse behavioural or psychological features are at risk of further severe or fatal attacks:

- Determine reason(s) for exacerbation and admission.
- Send details of admission, discharge and potential best PEF to GP.

***Salbutamol (Infusion solution 5 mg/5 ml)**

**N.B.** There are two formulations of salbutamol available for parenteral use. The infusion formulation, NOT the IV injection formulation, should be used to prepare infusions.

**Dose** – Initially 5 microgram/minute adjusted according to response and heart rate, usually in the range 3 - 20 microgram/minute.

**Administration** – Dilute 5 ml of solution with 500 ml glucose 5% or sodium chloride 0.9% to give a concentration of 10 microgram/ml

**Table 1 – Infusion rates for salbutamol**

| Dose | Infusion Rate |
|---|---|
| (microgram/minute) | (ml/hour) |
| 3 | 18 |
| 5 | 30 |
| 8 | 48 |
| 10 | 60 |
| 15 | 90 |
| 20 | 120 |

Please refer all patients admitted with a new diagnosis or exacerbation of asthma to the respiratory nurse specialists for education and inhaler technique prior to discharge.

For peak expiratory flow in normal adults, see chart on page 133.

# Management of Chronic Obstructive Pulmonary Disease (COPD)

## Introduction

COPD is a chronic, usually progressive disorder, characterised by airflow obstruction with little reversibility and usually > 20 pack years of smoking. Referral for a chest opinion is indicated in those with no or minimal smoking history, or age less than 40 years. Treatment for COPD is used to decrease symptoms and/or complications. Dyspnoea is the reason most patients seek medical attention and is a major cause of disability and anxiety associated with the disease.

## Assessment / monitoring

- Dyspnoea / exercise tolerance
- Spirometry
- Oximetry
- Weight

## General management

- Smoking cessation has the greatest capacity to influence mortality in COPD and all patients with COPD should receive education and support relating to this (see Appendix 1).
- Pneumococcal vaccination (**once only**) and influenza vaccination (**annually**) should be offered to all patients with COPD.
- A stepped approach with increases in treatment according to severity of disease is taken in the pharmacological management of chronic COPD. (The step down approach used in asthma is not applicable as COPD is a progressive disease).
- Patients with exertional dyspnoea (MRC grade 3/5 or more) should be considered for pulmonary rehabilitation.
- Peripheral oedema may indicate the development of *cor pulmonale* and the need for long-term oxygen therapy. If oxygen saturation < 92% check ABG. If $PaO_2$ < 8 kPa refer to chest clinic to assess for long-term oxygen therapy.
- Patients with a BMI < 20 or significant (> 3 kg) unintended weight loss should be assessed for causes of weight loss, in particular the development of lung cancer, and referred for dietary advice.

## Drug therapy / treatment options

### Inhaler devices

Metered dose inhalers (MDIs) are first line, however, not all patients can use them. Spacer devices can improve lung deposition with MDIs. Some examples of inhalers which may be used are detailed on the next page; however the drug choice at each step may be determined by the appropriate inhaler device for the patient. Your clinical pharmacist or respiratory nurse specialist can assess the patient and advise on alternative inhaler devices if appropriate.

**Continues on next page**

**Drug therapy / treatment options continued**

### Table 1 : Inhaled treatment options for COPD

| | FEV1 > 50% | FEV1 ≤ 50% |
|---|---|---|
| **1st line inhaled treatment** | SABA | SABA |
| **2nd line inhaled treatment** | LAMA or LABA | LAMA or LCCI* |
| **3rd line inhaled treatment** | LAMA + LABA | LAMA + LCCI* |

* where patient has had 2 or more exacerbations in 12 consecutive months

### Notes:

- SABA = short-acting $Beta_2$ agonist e.g. **Salbutamol inhaler 2 puffs (200 microgram) as required.**
- LAMA = long-acting muscarinic antagonist e.g.
  - **Tiotropium Handihaler® (dry powder) 18 microgram once daily** or
- LABA = long-acting $Beta_2$ agonist e.g.
  - **Salmeterol evohaler 2 puffs (50 microgram) twice daily** or
  - **Formeterol 12 microgram twice daily.**
- LCCI = LABA + corticosteroid combination inhaler – choice can vary - see BNF / NHSGGC Formulary.
- If still symptomatic despite maximal inhaled therapy, consider adding oral theophylline and mucolytic therapy. Prescribe theophylline by brand name as the pharmacokinetic profiles of controlled preparations differ. Theophylline dose will need to be reduced if patient is treated with a macrolide or fluoroquinolone. See page 345 for monitoring advice.
- Consider long-term oxygen therapy (LTOT) in patients with $PaO_2 \leq 7.3$ kPa when stable, or > 7.3 kPa and < 8 kPa when stable and: secondary polycythaemia, peripheral oedema, nocturnal hypoxaemia or pulmonary hypertension, if they have stopped smoking.

# Acute Exacerbation of Chronic Obstructive Pulmonary Disease (COPD)

## Introduction

COPD is a chronic, usually progressive, disorder characterised by airflow obstruction with little reversibility and usually > 20 pack years of smoking. An acute exacerbation may be described as a worsening of a stable situation.

Common features are: increased -

- Dyspnoea
- Cough
- Sputum (volume or purulence)
- Wheeze

### Assessment / monitoring

- Arterial blood gases (document oxygen therapy)
- CXR
- ECG
- U&Es, LFTs, and CRP
- FBC
- Theophylline level (if patient on theophylline)

The differential diagnosis includes:

- Pneumonia, pneumothorax, pulmonary embolus
- Left ventricular failure
- Lung cancer

# Treatment options

## Treatment: immediate

- **Oxygen 28% via venturi mask until gases checked – then titrate according to arterial blood gases.**

  Aim for $PaO_2$ > 7.5 kPa but < 10 kPa. If worsening respiratory acidosis or hypercapnia occurs, despite achieving target oxygen levels and adequate immediate therapy, ventilation (see page 141) may be indicated.

- Bronchodilators

  - Nebulised: Nebulisation should be with air. Supplementary oxygen (1 - 6 L/min to maintain oxygen saturation 88 - 92%) can be given by nasal cannula during nebulisation. If air driven nebuliser is not available, use up to 6 L/min of oxygen for a maximum of 10 minutes to drive nebuliser. Use a mouth-piece or close fitting mask to avoid risk of acute angle-closure glaucoma with ipratropium.

  **Salbutamol 5 mg nebules four times daily (but can be given up to 2 hourly as needed)**

  **Ipratropium 0.5 mg nebules four times daily (add if poor response to salbutamol *and if also on tiotropium, withold the tiotropium*)**

  - IV bronchodilators: Aminophylline may be considered if there is no response to nebulised therapy.

  **N.B.** The evidence for aminophylline is not conclusive although individual patients may benefit. Discuss with senior doctors. Side effects include nausea, seizures and it can precipitate arrhythmias.

  **Aminophylline infusion – dose administration and monitoring guidance see appendices 2 and 3.**

- Corticosteroids:

  **Prednisolone oral 30 mg - 50 mg each morning, for 7 days.** (Refer to local unit protocols for more detail) or if patient is unable to take oral treatment give:

  **Hydrocortisone IV 100 mg immediately then review, and if there is a need to continue IV therapy, prescribe 50 - 100 mg 6 - 8 hourly.**

- Antibiotics: Indicated in the presence of purulent sputum, raised inflammatory markers or focal radiological changes. They should be given orally unless there is a clinical reason for giving IV antibiotics. Send sputum for microscopy and culture. For antibiotic choice and course duration see page 230.

  **Note:** Serious drug interactions with clarithromycin (see BNF Appendix 1) and QTc prolongation.

- DVT Prophylaxis :

  **Enoxaparin SC 40 mg once daily (reduce to 20 mg daily if eGFR < 30 ml/minute/1.73m$^2$).**

- Physiotherapy: but **N.B.** there is no data to support emergency call out.

**Continues on next page**

**Treatment options continued**

- If persistent acidotic hypercapnic ventilatory failure despite optimal medical therapy consider discussion with ITU and/or non-invasive ventilation (NIV) - see protocol on next page)
- Mucolytic therapy may be of symptomatic benefit in patients where sputum clearance is troublesome:

  **Carbocisteine oral 750 mg three times daily then reduced to 1.5 g daily in divided doses as condition improves.**
- **Nicotine replacement therapy if appropriate (see Appendix 1).**
- Consider for referral to early supported discharge team (British Lung Foundation Nurses).

## Prior to discharge

1. Check inhaler technique and drug regimen: stop nebulised bronchodilator for 24 hours prior to discharge (if not used at home and not discharged under early supported discharge protocol). Home nebulisers should not be introduced as routine treatment immediately after acute exacerbation.
2. **Prednisolone oral 30 mg - 50 mg each morning for 7 days, without dose tapering, will be suitable for most patients.**

   **N.B.** There may be circumstances however where a tapering dose is necessary, e.g. in patients who are oral steroid dependent. In such circumstances reduce the dose to the normal maintenance dose or 10 mg daily (whichever is the greater) with a plan for early outpatient review or refer to local unit protocol.

   *Clinical improvement with oral steroids in acute COPD does not indicate need for long-term inhaled steroid.*
3. Physiotherapy advice regarding pulmonary rehabilitation.
4. Smoking cessation advice and referral if appropriate (see Appendix 1).
5. Home oxygen is usually assessed as an outpatient when patients are stable for at least 6 weeks post exacerbation and an ex-smoker or non-smoker.
6. Ensure optimal inhaled medication prior to discharge (see page 137).

# Non-Invasive Ventilation (NIV) Protocol in COPD

**AIM = To ensure patients are correctly and promptly identified as candidates for NIV.**

## Step 1

- History
- Examination
- CXR
- Arterial Blood Gases (ABGs)

**Is the patient a candidate for NIV?**

- Does the patient have a diagnosis of COPD?
- Does the patient have an acidotic exacerbation of COPD?
- If 'NO' to either of the above then discuss with senior medical staff suitability for NIV.
- Physiological criteria: decompensated type 2 respiratory failure i.e. pH < 7.35 ($H^+$ > 45 nmol/L) and $pCO_2$ > 6 kPa.
- On maximum medical therapy (and has been for 1 hour), nebulised salbutamol when required, corticosteroids, antibiotics if appropriate, controlled $FiO_2$ (usually 28% venturi mask – aim for $O_2$ saturation 86 - 90%), and reversal of respiratory depressants.
- Moderate to severe dyspnoea, RR > 25 bpm.

## Step 2 – Are there any contraindications to NIV?

**Absolute contraindications:**

- Respiratory arrest / need for immediate intubation
- Facial trauma / burns / surgery / abnormalities
- Fixed upper airway obstruction
- Severe vomiting
- Acute severe asthma
- Pneumothorax (unless chest drain inserted)

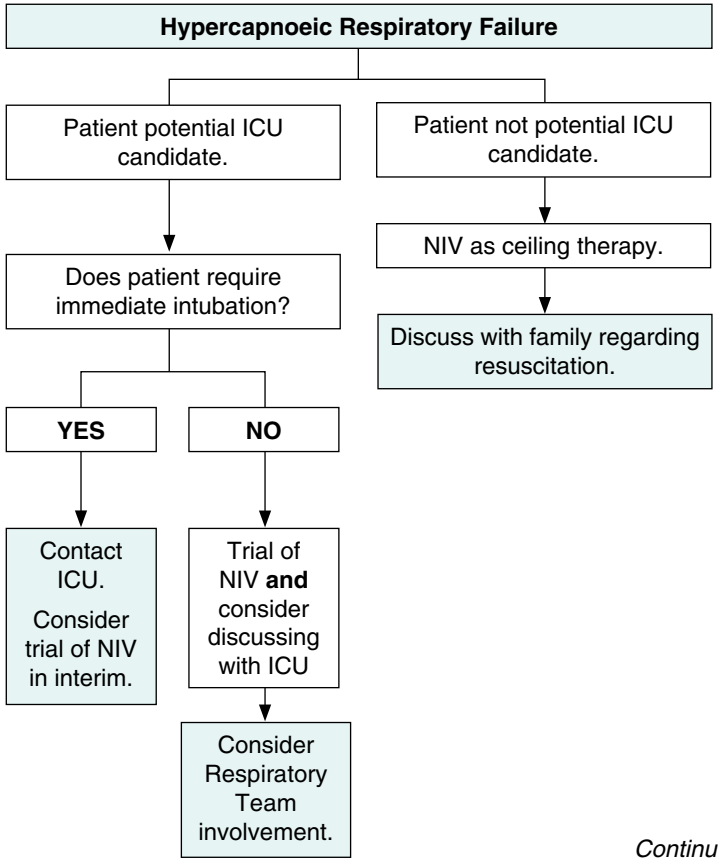
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**Relative contraindications:**

- Inability to protect airway
- Life-threatening hypoxaemia
- Haemodynamic instability
- Impaired consciousness
- Confusion / agitation
- Bowel obstruction
- Recent facial / upper airway or upper GI tract surgery
- Copious respiratory secretions
- Pneumonia

(NIV may be used despite 'relative contraindications' if this is the 'ceiling' of treatment and the patient is not for ICU / intubation.)

## Step 3 – Patient for ICU / intubation?




*Continues on next page*

## Step 4 – Initiation of NIV

**AIM =** To ensure patients are correctly and safely initiated on NIV.

*Arterial blood gases must be checked prior to starting NIV and whilst the patient is on controlled $FiO_2$.*

1. Size for face mask (select the smallest mask that fits comfortably):
   - small leaks are permitted but not into the eyes.
   - assess mask fit by monitoring mask leak, aim to keep any leaks to a minimum.
   - demonstrate use of quick release strap.
2. Position the patient in bed or chair at > $30^{O}$ angle.
3. Set ventilator settings:
   a. IPAP = 10 cm $H_2O$.
   b. EPAP = 4 cm $H_2O$.
   c. RATE = 12 bpm (becomes active should patient stop breathing or have periods of apnoea).
   d. EXPIRATION TRIGGER = 1.
   e. INSPIRATION TRIGGER = 1.
   f. RISE TIME = 5.
   g. OXYGEN = if supplementary oxygen required, set at 4 L/min and titrate as necessary to maintain $SpO_2$ 88 - 92%.
4. Increase IPAP in increments of 2 cm $H_2O$ to the maximum that patient will tolerate (usually not more than 20 cm $H_2O$).

## Step 5 – Monitoring the patient on NIV

*Record observations on NIV Observation Chart every 15 minutes for the first hour, evaluate thereafter:*

- $SpO_2$ – continuous monitoring with pulse oximeter.
- ABGs – 1 hour post commencement of NIV, thereafter evaluate as per patient's condition (if ABGs worsening after 4 - 6 hours then this is a poor prognostic factor for NIV).
- Respiratory rate.
- Heart rate.
- Evaluate accessory muscle use.
- Chest wall movement (to ensure adequate ventilation).
- Synchrony with the ventilator and air leaks.

*Continues on next page*

## Step 6 – Treatment failure

- Indications of failure:
  - No improvement in acidosis
  - No improvement in $CO_2$
  - No reduction in respiratory rate
  - Patient not tolerating
  - Patient refusal
- If patient is not tolerant of, or refuses NIV, rediscuss management with senior medical staff.
- *If ceiling of treatment and NIV fails, refer to palliative care guidelines on: www.palliativecareguidelines.scot.nhs.uk.*
- *Ensure documentation of patient and family views.*

## Step 7 – Weaning criteria

Is the patient ready to wean?

- Clinically stable for > 6 hours
- RR < 24 bpm
- HR < 110 bpm
- $H^+$ < 45 nmol/L
- $SpO_2$ > 88% on 4 L $O_2$ whilst on NIV

**If 'NO' to the above:**

- Continuous NIV (monitor as before)

**If 'YES' to the above:**

- Allow breaks for meals, medication, physiotherapy etc
- Consider nocturnal NIV only
- Controlled $O_2$ therapy

*If worsening respiratory distress, reassess patient, review therapy and consider recommencing NIV.*

## Patients on home NIV

Some patients use NIV chronically at home. Typical reasons are:

- Chronic hypercapnic respiratory failure:
  - obesity hypoventilation
  - chest bellows disease
  - neuromuscular disease
  - occasionally COPD
- Palliation in motor neurone disease (MND / ALS)

The local respiratory unit should be involved early in the care of these patients.

# Investigation of Unilateral Pleural Effusion

## Introduction

Pleural effusions, the result of the accumulation of fluid in the pleural space, are a common medical problem. They can be caused by several mechanisms including increased permeability of the pleural membrane, increased pulmonary capillary pressure, decreased negative intrapleural pressure, decreased oncotic pressure, and obstructed lymphatic flow.

Pleural effusions are classified into transudates and exudates:

- A transudative pleural effusion occurs when the balance of hydrostatic forces influencing the formation and absorption of pleural fluid is altered to favour pleural fluid accumulation. The permeability of the capillaries to proteins is normal. (Common causes – left ventricular failure (LVF), liver cirrhosis, hypoalbuminaemia and peritoneal dialysis).
- In contrast, an exudative pleural effusion develops when the pleural surface and/or the local capillary permeability are altered. (Common causes – malignancy and parapneumonic effusions).

## Assessment / monitoring

- The differential diagnosis of an effusion is wide, and may include pulmonary, pleural or extrapulmonary disease. Please contact local Respiratory team early to guide aspiration and further systematic investigation and management (see flow diagram on next page).
- According to Light's criteria an effusion is an exudate if any one of the following is true of pleural fluid aspirate:

  - Pleural total protein: serum total protein > 0.5

  - Pleural LDH: serum LDH> 0.6

  - Pleural LDH > 0.66 upper limit normal range in your hospital.
- An accurate drug history should be taken during clinical assessment. Although uncommon, a number of medications have been reported to cause exudative pleural effusions. Discuss with a respiratory physician or your clinical pharmacist if necessary.
- Aspiration should not be performed for bilateral effusions in a clinical setting strongly suggestive of a pleural transudate, unless there are atypical features or they fail to respond to therapy.

## Safety and timing of pleural procedures

- Current BTS guidance recommends the use of bedside pleural ultrasound at the time of procedure where available to guide the site of pleural aspiration and chest drain insertion for pleural effusion. The aim is to reduce complications from perforation of viscera.
- Diagnostic / therapeutic aspiration should occur during normal working hours where possible, unless urgently indicated (e.g. large effusion causing significant breathlessness or hypoxia).
- Avoid chest drain placement out of hours if possible unless empyema present on diagnostic tap. Removal of all fluid prior to definitive diagnosis may delay further investigations and definitive management, especially of possible malignant effusions.

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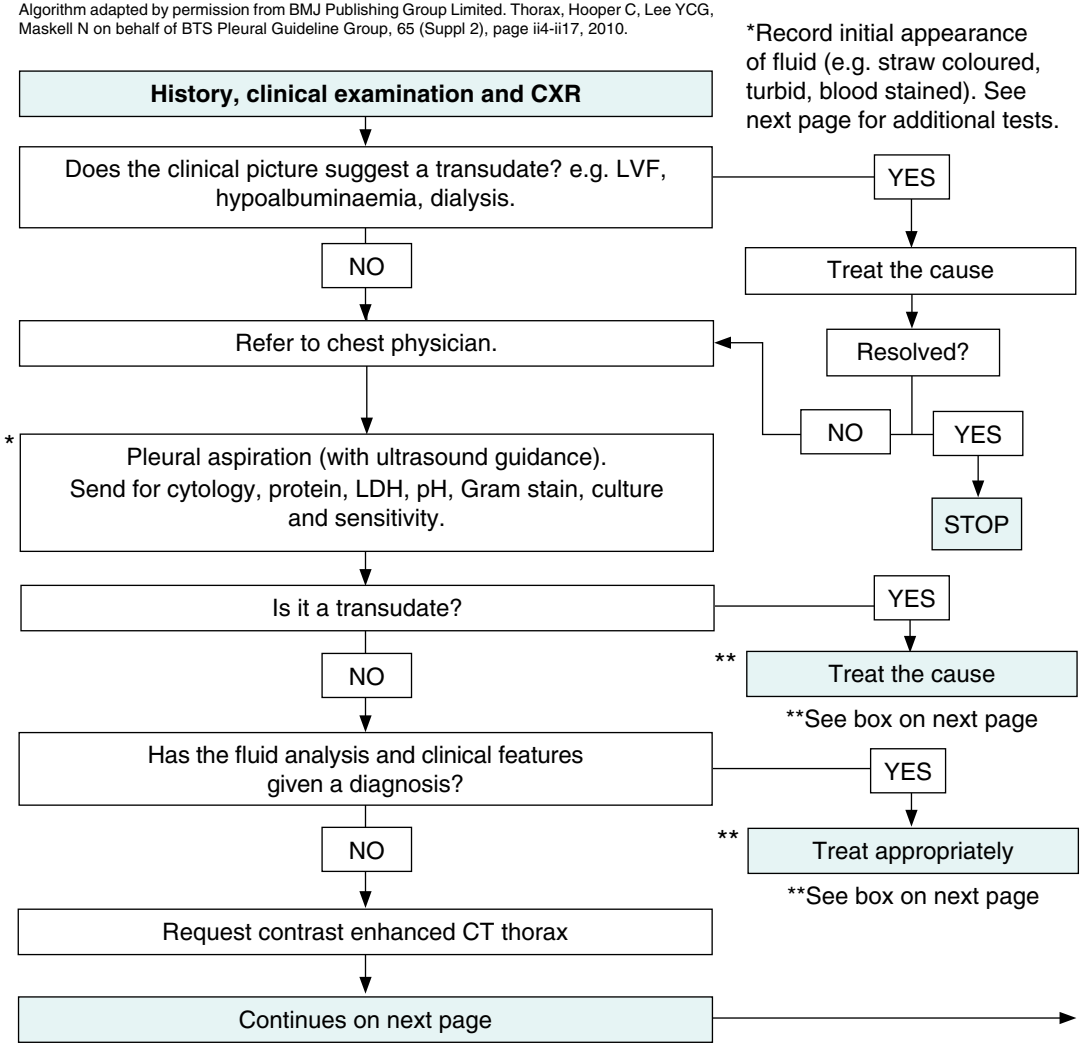
- Anticoagulation (raised prothrombin time, warfarin), low platelets (< 50 x $10^9$/L), low molecular weight heparin (enoxaparin, dalteparin) and clopidogrel are relative contraindications to pleural aspiration / drainage and the procedure should be delayed until these factors are corrected, unless required as an emergency. Aspirin alone is not a contraindication to pleural procedures.

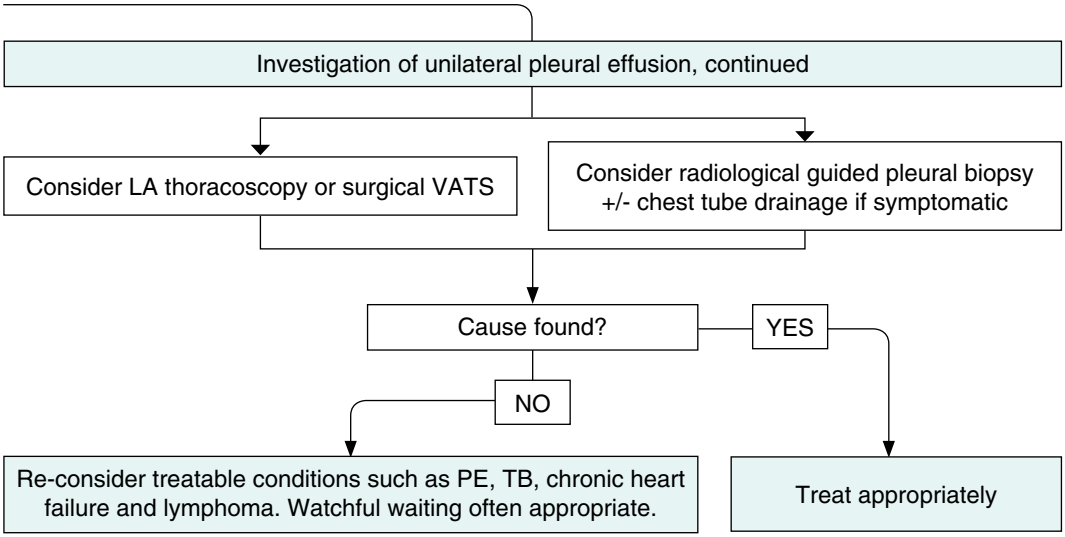
## General management

This aim of this guideline is to assist in the **investigation** of pleural effusion. Treatment is dependent on the cause e.g. if the cause is found to be pulmonary embolism then refer to the guideline for **treatment** of DVT / PTE (page 71).

## Investigation of unilateral pleural effusion

Algorithm adapted by permission from BMJ Publishing Group Limited. Thorax, Hooper C, Lee YCG, Maskell N on behalf of BTS Pleural Guideline Group, 65 (Suppl 2), page ii4-ii17, 2010.






| Suspected cause | Test results | Management |
|---|---|---|
| Parapneumonic | Straw coloured exudate<br>Normal pH / glucose | Treat as pneumonia<br>Therapeutic aspirate / drainage if large / symptomatic |
| Complicated parapneumonic | May look opaque / turbid<br>Acidic (pH < 7.2) Glucose < 2.2 mmol/L | Treat as pneumonia<br>Early drainage – risk of progression to empyema |
| Empyema | Frank pus / organisms on gram film. Positive culture | Discuss antibiotics with microbiology<br>Urgent drainage (same day) |
| Malignant (lung, mesothelioma, lymphoma, breast most common) | Often bloodstained<br>(if in doubt – haematocrit)<br>Normal pH. High LDH<br>Send for cytology (as much as possible) | **Do not drain** until discussed with Respiratory.<br>Therapeutic aspirate if symptomatic.<br>Further investigation and definitive management may be affected if drained. |
| Chylothorax (e.g. post thoracic surgery / injury, haem malignancy) | Looks like milky tea<br>Test for cholesterol and TGs<br>Consider flow cytometry if available. | **Do not drain** until discussed with Respiratory.<br>Therapeutic aspirate if symptomatic. |
| Rheumatoid | Turbid fluid<br>Very low pH / glucose. Very high LDH | Discuss with Respiratory and/or Rheumatology<br>May mimic empyema – if in doubt treat as this |
| Tuberculous | Normal pH / glucose<br>Ensure sample for AAFB sent | **Do not drain** until discussed with Respiratory. |

# Management of Pneumonia

## Introduction

Pneumonia may be classified as Community Acquired (present on admission to hospital or developing within 48 hours of admission) or Hospital Acquired (developing at least 48 hours after admission or within 10 days of discharge). Pneumonia is defined as features of respiratory infection (cough, purulent sputum, fever, pleurisy, with new focal abnormalities on respiratory examination or CXR).

## Assessment / monitoring

The CURB-65 score predicts 30 day mortality and is a useful tool to support decisions regarding admission and management of community acquired pneumonia (see page 150 for flow diagram and page 231 for CURB-65 criteria). It should be used in conjunction with SIRS criteria (page 211) and should aid clinical judgement, not replace it. It is not used for aspiration pneumonia or infective exacerbations of asthma / COPD.

### Immediate investigations:

- Assess Airway, Breathing and Circulation and then give oxygen therapy as appropriate (see under General management).
- Arterial blood gas if oxygen saturations < 95% on air.
- BP – Give fluid challenge if hypotensive (systolic < 90 mmHg), 250 ml over 15 minutes with repeat BP every 15 minutes. Clinically review if no response to 1L fluid.
- FBC, U&Es, LFTs, CRP, blood cultures, sputum culture and sensitivity.
- EDTA sample of blood for multiplex PCR for pneumococcal and *Haem influenzae* DNA detection.
- CXR (lobar / bronchopneumonia)
- ECG
- Urine for *Legionella* and pneumococcal Ag
- Consider possibility of *M. tuberculosis*, particularly in upper lobe or cavitating disease – request sputum AFB as emergency.
- Respiratory secretions / mouthwash to virology if possibility of atypical or viral pneumonia.

### Further investigations:

- Nasopharyngeal aspirates / washings.
- Broncho-Alveolar Lavage (BAL) and tracheal aspirate or sputum for viral PCR.
- Throat swab in viral transport fluid may be sent (but less useful than samples listed above).
- Ensure travel history and contacts established (including animal and occupational).

*Continues on next page*

## General management

- Oxygen as appropriate to achieve target oxygen saturations as follows:
  - 94 - 98% for most patients
  - 92 - 96% may be acceptable if > 70 years old
  - 88 - 92% for those with COPD or at risk of hypercapnic respiratory failure (e.g. morbid obesity, neuromuscular or chest wall disease).
- Antibiotics as per flow diagram on next page - **start immediately.** Consider changing to appropriate antibiotic if specific organism identified.
- IV fluids (fever / excess fluid loss)
- Analgesia for pleuritic pain (NSAIDs if not contraindicated).
- Physiotherapy if copious secretions.
- Consider nursing patient in high dependency unit if severe.
- Low molecular weight heparin prophylaxis for DVT (see page 66)
- Repeat CXR and CRP and consider early respiratory referral if not improving within 3 days, atypical features, or effusion / empyema suspected.

## Treatment options

Community acquired pneumonia (CAP) studies show increased mortality in young patients when antibiotic treatment is delayed. Prescribe antibiotic for **immediate administration.** The flow diagram on the next page outlines the general management of CAP; calculate CURB-65 score first (see page 231) before prescribing.

| Pneumonia | Management |
|---|---|
| Hospital acquired | See page 234 |
| Suspected *Staphylococcus aureus* pneumonia (e.g. IVDA, post influenzae or chicken pox) | See page 235 |
| Aspiration pneumonia | See page 235 |
| *Legionella* pneumonia | If confirmed, discuss with microbiology to guide antibiotic choice. If severe consider extending treatment up to 14 - 21 days |
| Cavitating pneumonia of any type | Discuss with local Respiratory Team early on. Consider *Staphlyococcus, Streptococcus*, tuberculosis, Gram-negative (e.g. *Klebsiella*) and non-infectious causes (lung cancer, vasculitis). |

For oral step down – see page 205 IVOST guideline

NIV / CPAP should not be used for respiratory failure in pneumonia outside of an ITU setting as delayed transition to invasive ventilation (if required) increases mortality. If ITU admission is not appropriate due to comorbidities then NIV / CPAP on the ward could be considered as ceiling of treatment.

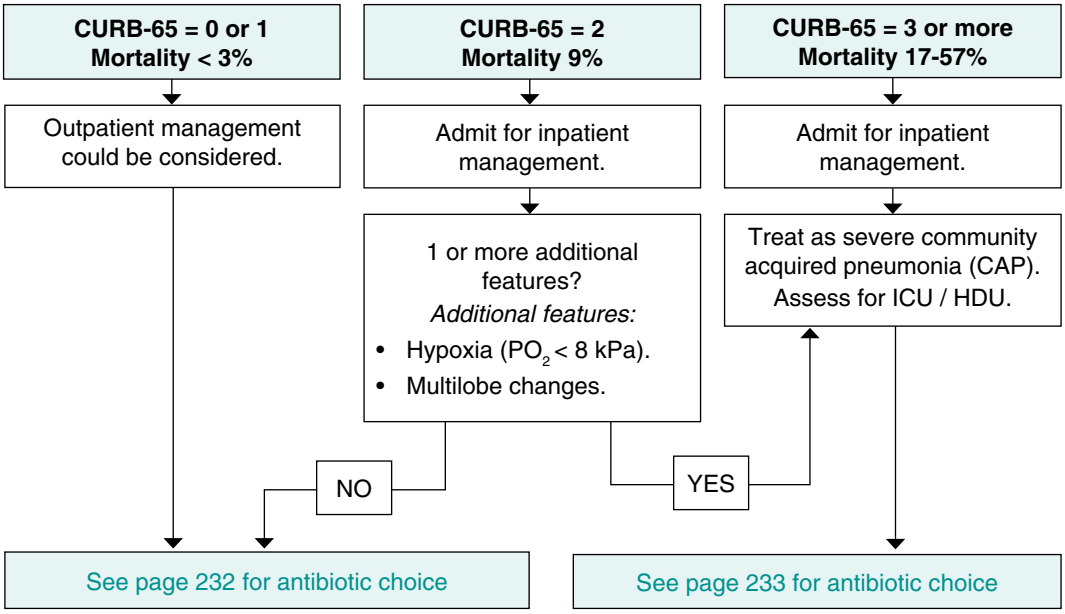
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**Treatment options continued**

### Discharge planning

- Consider discharge when off oxygen and on oral antibiotics > 24 hours, CRP falling and clinical improvement (temperature < 37.3°C, RR < 24 breaths/minute, HR < 100 bpm, systolic BP > 90 mmHg).
- Follow up and repeat CXR required at 6 - 8 weeks post discharge.

## Antibiotic Choice Based on CURB-65 Score




**Note:** Serious drug interactions with certain antibiotics, see page 204. Further information can be found in Appendix 1 of BNF.

# Management of Pneumothorax

## Introduction

Pneumothorax is defined as air in the pleural space – that is, between the lung and the chest wall. Primary spontaneous pneumothoraces arise in otherwise healthy people without any lung disease. Secondary spontaneous pneumothoraces arise in subjects with underlying lung disease. By definition, there is no apparent precipitating event in either.

## Assessment / monitoring

- In both primary and secondary spontaneous pneumothoraces the diagnosis is usually established by plain chest radiography. (Expiratory chest radiographs are not recommended for the routine diagnosis of pneumothorax).
- A lateral chest or lateral decubitus radiograph should be performed if the clinical suspicion of pneumothorax is high, but a CXR is normal.
- CT scanning is recommended when differentiating a pneumothorax from complex bullous lung disease, when aberrant tube placement is suspected, and when the plain chest radiograph is obscured by surgical emphysema.
- The clinical history is not a reliable indicator of pneumothorax size.

## General management

- The flow diagrams for primary and secondary pneumothoraces provide a systematic approach to treatment decisions.
- Remember that breathless patients should not be left without intervention regardless of pneumothorax size on chest radiograph.
- There is no evidence that large chest drains are more effective except in trauma. Smaller drains (e.g. $\leq$ 16 Fr) are easier to insert and better tolerated by the patient.
- Ideally patients with chest drains should be managed in a ward used to dealing with them (e.g. respiratory ward) to minimise complications.

## Treatment options

- Further treatment options include chest drain suction, chemical pleurodesis and thoracic surgery. If a pneumothorax fails to respond to treatment within 48 hours, prompt referral to a respiratory physician is essential so that these options may be considered.
- Persons with a second or recurrent pneumothorax should be referred for a respiratory opinion as pleurodesis and investigation for underlying lung disease may be indicated.
- Patients should be advised that they should not fly until the pneumothorax has resolved radiologically and for 6 weeks afterwards. They should further be advised to seek specialist medical advice prior to scuba-diving as this may be permanently contraindicated.

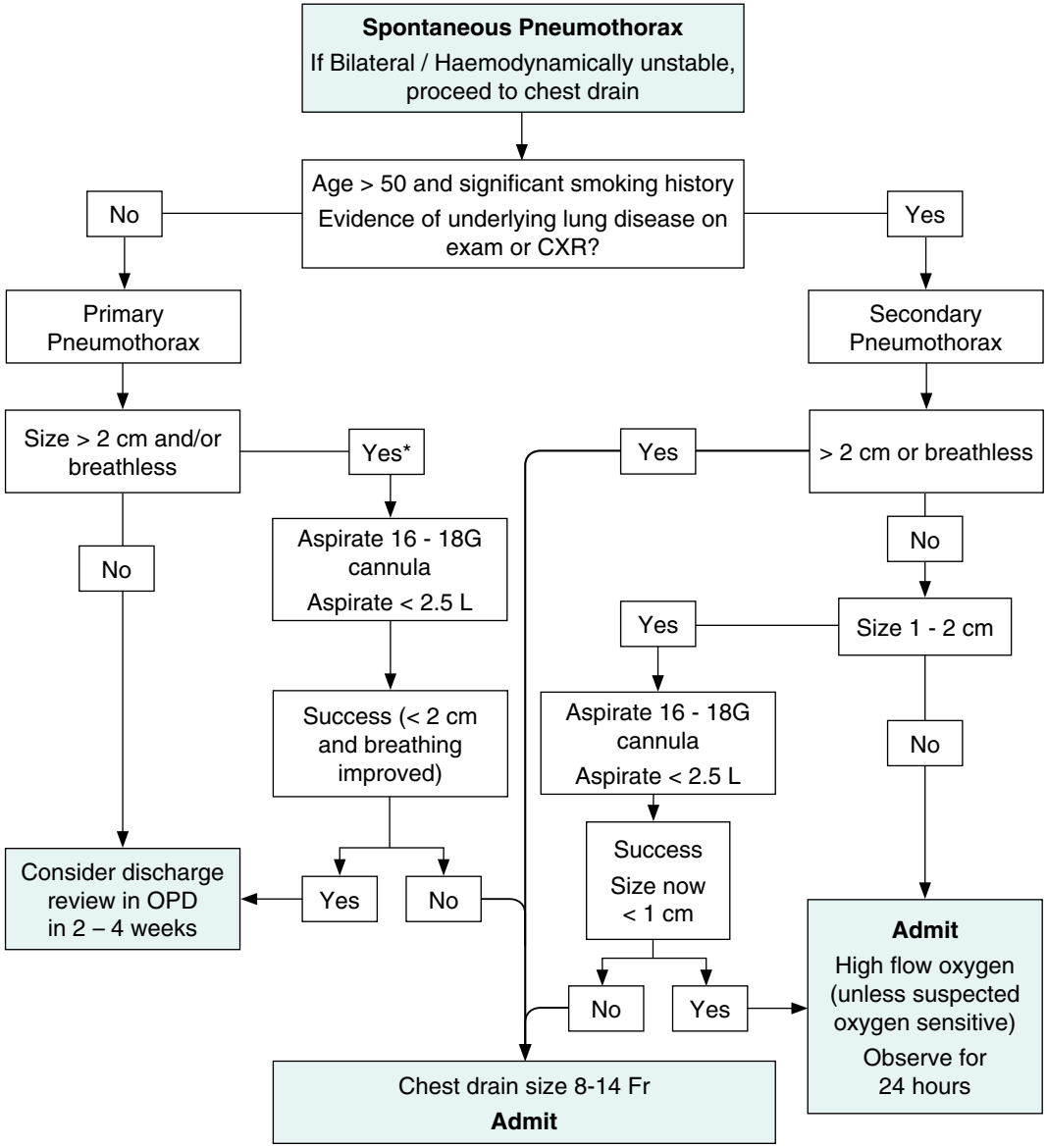
## Other

Strong emphasis should be placed on the relationship between the recurrence of pneumothorax and smoking in an effort to encourage patients to stop smoking.

*Continues on next page*

# Management of Spontaneous Pneumothorax

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# Management of Stridor

## Introduction

Stridor is an unusual, high pitched **inspiratory** sound which indicates significant airway obstruction and is usually caused by tracheal obstruction although can be a result of obstruction of the main bronchi. It is essential to distinguish it from other causes of dyspnoea as it signifies airway compromise.

Stridor represents an emergency situation and may require urgent ENT or Respiratory assessment. You may need to discuss the patient with ITU in order to secure the airway, particularly if the history is not clear cut. Discuss any patients with a Registrar or above immediately.

## Assessment / Monitoring

The initial assessment includes:

- Assess airways, breathing and circulation – immediate resuscitation as needed
- Oxygen saturations
- CXR – portable if patient not safe to go to department

Obtain full history including:

- The development of new or worsening respiratory symptoms
- Details of known malignancies and their treatment
- Co-morbidities
- Medication including use of and contraindications to corticosteroids

## Treatment / drug therapy

Treatment should include:

- **Oxygen (humidified if possible)**
- **Dexamethasone oral (unless swallowing problems then IV) 8 mg twice daily (morning and lunchtime)** if no contraindications and gastroprotection if appropriate (e.g. **Omeprazole oral 20 mg once daily or lansoprazole 30 mg once daily if no contraindications**).
- **Nebulised Salbutamol 5 mg when required**
- Treatment of any infection
- If severe and not improving on conservative management may need to **consider**
  - Tracheostomy if upper airway obstruction – discuss with oncall ENT
  - Nebulised adrenaline – discuss with senior doctor used to giving this e.g. ITU

Definitive treatment includes:

- Radiotherapy if appropriate – discuss with on-call clinical oncologist

- Laser / stenting for tracheal obstruction – discuss with local Respiratory team

**Continues on next page**

**Treatment / drug therapy continued**

If no other treatment options then make patient comfortable with sedation. ALWAYS discuss with senior member of team.

- Consider Heliox 80:20 if available (helium oxygen mix which is less viscous than air and easier to inhale past obstruction).

# Initial Management of Superior Vena Cava Obstruction

## Introduction

Superior Vena Cava Obstruction (SVCO) is an oncological emergency and any patients should be discussed with a Registrar or above immediately, and with the local Respiratory team or on-call Oncology team at the Beatson, as soon as possible to guide investigation and management.

SVCO results from the compression of the superior vena cava by either a tumour arising in the right main or upper lobe bronchus or mediastinal lymphadenopathy. Initially it is diagnosed clinically in the presence of neck and facial swelling and distended veins over the anterior chest wall. There may also be swelling of one or both arms and symptoms of dyspnoea and headache. Malignancy is the commonest cause (> 90%), most typically lung cancer, lymphoma, metastatic disease, mesothelioma and thymoma.

## Assessment / monitoring

The initial assessment includes:

- Obtain full history including:
  - Details of known malignancies and their treatment
  - The development of new or worsening respiratory symptoms, arm swelling and headaches, and rapidity of onset
  - Co-morbidities
  - Medication including use of and contraindications to corticosteroids and anticoagulation.

Examine for distended external and internal jugular veins, collateral veins on the anterior chest wall, facial, arm and neck swelling, and conjunctival redness.

- The investigation of choice is a contrast enhanced spiral or multi-slice chest CT (CTPA). This defines tumour extent, and often the site of occlusion or stenosis and the extent of any thrombus formation. Impending SVCO can be an incidental finding on CT.
- Confirmation of diagnosis by histology may involve fine needle aspirate of palpable nodes, bronchoscopy, or CT guided biopsy. Seek advice from Respiratory or Oncology as soon as possible to guide investigation and management.

In addition to above, questions that may influence whether the patient should be considered for SVC stent or chemotherapy / radiotherapy are:

- Is there a relative contraindication for radiotherapy? E.g. Previous chest / mediastinal radiotherapy? Is the patient able to lie reasonably flat?
- Performance status (0 = normal activity, 1 = restricted daily activity, 2 = ambulatory and self caring, out of bed > 50% of the day, 3 = capable of limited self care, in bed > 50% time, 4 = unable to self care, chair / bed-bound)
- Availability of stenting (performed by interventional radiology)

## Treatment / drug therapy

- Treatment is initially to alleviate symptoms and when known directed at the underlying cause.
- Ensure that the patient has no life-threatening symptoms (e.g. associated stridor) and is fit enough for active treatment.
- If no contraindication to corticosteroids commence:

  **Dexamethasone oral (unless swallowing problems then IV) 8 mg twice daily (morning and lunchtime)** with gastroprotection if appropriate (e.g. **Omeprazole oral 20 mg daily or lansoprazole oral 30 mg once daily if appropriate**).

  This may be commenced while waiting for CT if clinical suspicion of SVCO is high. If CT confirms SVCO continue dexamethasone and seek urgent advice. As symptoms improve, dose may be gradually reduced over several weeks. If symptoms do not improve after 7 days consider stopping. If the CT scan shows no SVCO then stop dexamethasone.
- Other treatments frequently used are radiotherapy, stent insertion and chemotherapy and will depend on clinical scenario. If thrombus is present consider anticoagulation if no contraindications (see guideline on LMWH for VTE in cancer on the Clinical Guideline Electronic Resource Directory on StaffNet).

Section 6

# Central Nervous System

# General Principles of Acute Pain Management

This guideline is aimed at providing quick and general guidance on acute pain management in adults, whether medical or surgical in origin. It does not replace the more detailed local guidelines available at each site, which should be referred to as appropriate. Contact your local Acute Pain Team for further advice.

For acute pain management in paediatrics, see Paediatric Analgesia in the Emergency Department guideline on StaffNet.

## Introduction

There is good evidence that effective pain relief reduces patient morbidity, helps facilitate early recovery, mobilisation and discharge from hospital. As pain is subjective, drug regimens need to be tailored to meet individual requirements. There are local variations in which particular drugs from each class of analgesics may be preferred and may be indicated in a specialty specific analgesic ladder.

## Assessment / monitoring

- Pain should be considered the fifth vital sign. It should be assessed on movement and the pain score recorded when routine observations are carried out.
- Use pain scores to assess initial analgesic requirements and the effects of treatment. Ensure the scores are documented.
- For post-operative pain monitor pain regularly. This should begin as soon as the patient is admitted to the recovery room and continued onto the ward thereafter.
- If pain scores are increasing **always** consider that there may be a reason for this e.g. worsening of condition, presence of wound infection, constipation, etc.

**N.B.** Pain assessment tools will vary between hospitals in NHSGGC.

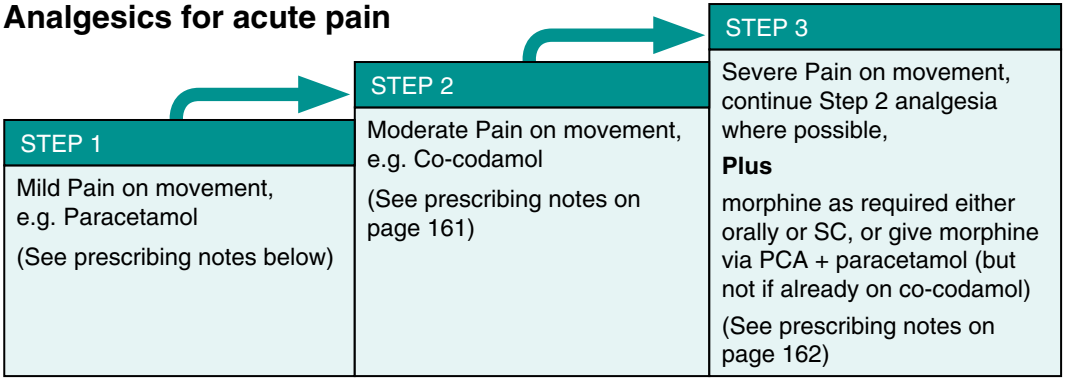
## Treatment options

**Some general principles of acute pain management:**

- Before prescribing, ascertain whether patient is intolerant to any analgesic. If intolerant to opioid, establish which one as most patients are not intolerant of every opioid.
- Prescribe analgesia **regularly** according to guidelines on the next page or as per local guidelines, bearing in mind any documented sensitivities / allergies.
- Review analgesia at least daily and always at discharge.
- If an analgesic has failed to control the pain, step up to the analgesic on the next step of the ladder – it is pointless to try another analgesic of similar strength. For example, if a patient has pain not controlled by co-codamol 30/500 mg, prescribe a strong opioid such as morphine.
- Consider the available routes of administration. Use the oral route whenever possible and appropriate.
- Remember that analgesia can be **stepped down** as well as up.
- Consider the potential side effects of analgesia.

*Continues on next page*

## Analgesics for acute pain




Consider addition of NSAID if:

- No history of peptic ulceration.
- No renal impairment.
- No bleeding problems.
- No asthma.
- No aspirin sensitivity.

## Analgesics for acute pain – prescribing notes

### Step 1. Paracetamol

- Is an effective analgesic for mild to moderate pain
- Improves the effect of other analgesics in the treatment of moderate to severe pain.

**General cautions:**

- Haematology / ICU patients where pyrexia of sepsis may be masked.
- Hepatic failure (see below under each preparation)
- Renal impairment (see under IV preparation below)
- Low weight (see under IV preparation below)
- Do not use different routes of administration of paracetamol at the one time

**Paracetamol oral: 1 g four times daily (max dose). Consider dose reduction in patients with low body weight (≤ 50 kg), renal / hepatic impairment or glutathione deficiency (chronic malnourishment, chronic alcoholism) to 15 mg/kg/dose up to four times daily (max 60 mg/kg/day). An example is: paracetamol oral 500 mg four times daily.**

**Paracetamol IV**

**Indication**: Short-term treatment of moderate pain following surgery, and for the short-term treatment of fever, when administration by IV route is clinically justified. Paracetamol IV is not more effective than oral paracetamol. If used, change to oral route as soon as possible. There are prescribing restrictions with IV paracetamol – aquaint yourself with local practice before prescribing.

**Dose**: Varies – dependent on weight, renal function and other co-morbidities. See general caution above, notes and dosing tables on the following page to determine dose.

**Continues on next page**

**Paracetamol IV continued**

**Administration**: Infuse ready-made solution over 15 minutes. For doses < 1 g, remove and discard excess drug / volume then administer required amount from vial.

**Important notes for IV paracetamol:**

- Low weight (≤ 50 kg) or renal impairment (CrCl ≤ 30 ml/minute) dose reduce using the tables below.
- Maximum daily dose of paracetamol IV must not exceed 3 g per day in patients with:
  - hepatocellular insufficiency
  - chronic alcoholism
  - chronic malnutrition (low reserves of hepatic glutathione)
  - dehydration
- In overdose, paracetamol IV may possibly be more toxic than the oral route. See TOXBASE www.toxbase.org (password required) for management.

**Table 1 – IV Paracetamol dosing table**

| Patient group | Dose | Dosage interval | Maximum daily dose |
|---|---|---|---|
| Adults > 50 kg | 1 g up to four times daily | 4 hours | 4 g |
| Adults ≤ 50 kg | 15 mg/kg per administration (see Table 2) | 4 hours | 60 mg/kg without exceeding 3 g |
| Renal impairment with creatinine clearance ≤ 30 ml/minute | As above, depending on weight (see Table 2) | 6 hours | As above, depending on weight |

**Table 2 – IV Paracetamol dose for patients ≤ 50 kg**

| Weight (kg) | Dose (mg) | Volume (ml) |
|---|---|---|
| 30 - 34 | 500 | 50 |
| 35 - 39 | 550 | 55 |
| 40 - 44 | 650 | 65 |
| 45 - 50 | 700 | 70 |

**Continues on next page**

**Analgesics for acute pain – prescribing notes continued**

### Step 2. Weak opioid analgesics for moderate pain

**Co-codamol* oral 30/500 mg 1 - 2 tablets four times daily (max 8 tablets in 24 hours) or**

**Codeine oral 30 - 60 mg four times daily (max 240 mg/day orally) or**

**Dihydrocodeine oral 30 mg four times daily (max 120 mg/day orally).** Dihydrocodeine 60 mg will provide little additional analgesia but more pronounced side effects.

**or**

**Tramadol oral 50 - 100 mg four times daily.**

**Notes:**

- *Co-codamol contains paracetamol. Certain patients groups may require a dose reduction (see page 159 for details).
- Tramadol should not be used routinely. In particular it **should not** be used as breakthrough analgesia when patients are already prescribed Step 2 opioids.
- Where possible co-prescribe a stimulant laxative (see page 45).

### Adjuvants: NSAIDs (Non-Steroidal Anti-Inflammatory Drugs):

**Ibuprofen oral 400 mg three times daily.** Rarely will 800 mg three times daily be required as there is very little additional benefit but an increase in side effects

**or**

**Naproxen oral 250 - 500 mg twice daily or**

**Diclofenac oral / rectal / IV 50 mg three times daily.**

Adding NSAIDs can be beneficial and may reduce opioid requirements. They can be used at any step of the analgesic ladder.

**Caution with NSAIDs:**

- Age > 70 years
- If patients are at risk of gastrointestinal mucosal damage (elderly, previous ulcer history, dyspepsia, also on steroids) but still need NSAIDs, prescribe gastric protection with a proton pump inhibitor:
  **omeprazole oral 20 mg daily or**
  **lansoprazole oral 15 - 30 mg daily.**
- Consider the patient's overall condition and concomitant medication e.g. hypovolaemia, hypotension, heart failure, other nephrotoxic medication.
- NSAIDs may be associated with a small increased risk of thrombotic events, particularly when used in high doses and for long-term treatment. Use the lowest effective dose for the shortest period possible.

**Avoid NSAIDs:**

- In patients with bleeding or past history of upper GI ulceration, aspirin-sensitive asthma, renal insufficiency including oliguria.
- In patients taking warfarin or aspirin.
- In severe heart failure

**Continues on next page**

### Step 3. Strong opioids for severe pain

**Morphine oral:**

| Age | Initial Dose |
|---|---|
| ≤ 70 years | 10 mg every 1 - 2 hours (regularly monitor / review sedation score and respiratory rate). |
| > 70 years | 5 mg every 1 - 2 hours (regularly monitor / review sedation score and respiratory rate). |

**Morphine IV – post-operative administration:**

| Age | Dose |
|---|---|
| < 65 years | 1 - 2 mg at 5 minute intervals, up to a maximum of 10 mg then reassess |
| 65 - 80 years | 1 mg at 10 minute intervals |
| > 80 years | 0.5 - 1 mg at 10 minute intervals |

## General notes on morphine

- Morphine should be prescribed on an age-related basis rather than weight-related.
- Adding paracetamol and/or an NSAID can reduce opioid dose requirements and enhance analgesic effect of morphine.
- Titrate dose of morphine to response, monitor closely for oversedation and respiratory depression (refer to page 41)
- Co-prescribe a stimulant laxative (see page 45 on Management of Constipation).
- Co-prescribe an antiemetic. Patients with a history of post-operative nausea and vomiting (PONV) or who are at high risk may particularly benefit from prophylactic antiemetics (see page 164 on Management of PONV).

**Caution:**

- In renal and hepatic impairment seek dosing advice from your ward pharmacist or senior member of staff.

### Notes on parenteral morphine

- For subcutaneous morphine (acute, pre- or post-operative pain) refer to local protocols.
- Use IV only to initiate analgesia, or as PCA. It should not be used as breakthrough analgesia and patients must be closely monitored during and after administration for oversedation and respiratory depression.
- Consider oral morphine when parenteral morphine is discontinued.

**Continues on next page**

**Analgesics for acute pain – prescribing notes continued**

**Patient controlled analgesia (PCA) and epidurals**

- PCA and epidurals are prescribed by anaesthetists.
- For management of these patients refer to local guidelines or contact the Acute Pain Team for advice.
- Use the appropriate observation charts – note specific charts are available on some sites for patients with renal failure.

**Step down analgesia**

- Prescribe 'step-down' analgesia **before** epidural or PCA is discontinued.
- Whenever possible, ensure at least Step 2 analgesia is prescribed regularly, with a strong opioid prescribed for breakthrough pain.
- Further step down to paracetamol is usually possible within 3 days depending on pain scores.

## Pain management in patients on long-term methadone

Inadequate treatment of pain in methadone-maintained patients commonly leads to disruptive behaviour by angry and frightened patients who then may discharge themselves against medical advice, often to the detriment of the patient's health. For patients on long-term methadone contact the acute pain team.

Some general guidance until more detailed advice from a specialist can be sought:

- Methadone in maintenance doses does not have analgesic effects.
- Where possible do not interrupt daily methadone maintenance or change the patient's dose of methadone.
- Manage pain as described previously:
  - Opioids should be used as needed and in conjunction with non-opioid analgesia.
  - Titrate dose according to side effects and pain relief starting with a low dose initially, as the dose of methadone and the use of illicit drugs prior to admission may be unknown. Sedation scores are more sensitive than respiratory rate when asessing opiates.
  - These patients may eventually need higher and more frequent doses of analgesia.
- Do not use agonist / antagonist drugs such as pentazocine, buprenorphine.
- Cease the parenteral use of opioid analgesics as soon as possible and convert to oral preparations.
- These patients can be complex and their pain difficult to manage - contact the Acute Pain Team for further advice.

For opioid-induced side effects and management see page 41.

# Management of Postoperative Nausea and Vomiting (PONV)

This guideline is aimed at providing quick and general guidance on PONV. Refer to local protocols for more detailed guidance.

## Introduction

Nausea and vomiting is a common and distressing symptom or side effect in medicine, surgery and following anaesthesia. It can cause complications such as wound dehiscence, electrolyte imbalance, increased pain, dehydration and aspiration. Generally, uncomplicated PONV rarely goes beyond 24 hours post-operatively. Problematic PONV however is more multifactorial in origin and can be difficult to treat effectively. Patients at risk of this should be identified by the anaesthetist and may be given prophylactic antiemetic treatment. Post-operative patients with nausea and vomiting may be considered as either failure of prophylaxis or for primary treatment.

## Assessment / monitoring

- Regularly use PONV score to assess patient (scoring varies across NHSGGC hospitals).
- Assess hydration and perfusion
- Assess gastric emptying or paralytic ileus – consider nasogastric (NG) tube.
- Seek cause of PONV. Is it:
  - Inadequate pain relief, infection, hypovolaemia, hypoxia, hypotension, anxiety, removal or insertion of NG tube?
  - Has enough primary antiemetic been given? Check both anaesthetic and prescription charts.

## General management

- Minimise patient movement.
- Ensure analgesia is adequate – see previous guideline.
- Ensure good oxygenation and normal blood pressure.
- Give IV fluids if dehydrated.
- Administer antiemetic early when patient is nauseated rather than waiting for patient to vomit before treating PONV (see drug therapy section).
- If cause of PONV is known, correct if possible. For instance, postoperative opiates increase patient's risk of PONV so where possible consider other analgesics.

*Continues on next page*

## Drug therapy

The table below is a general quick guide on the prescribing of antiemetics, but see local guidelines.

| Antiemetic | Dose and route of administration | Site of Action |
|---|---|---|
| **Prochlorperazine** | 3 - 6 mg buccal every 12 hours or 12.5 mg deep IM as a 'one-off' dose (**never IV**).<br>In elderly use<br>3 mg buccal or 6.25 mg IM. | Medullary chemoreceptor trigger zone.<br>Dopamine (D2) receptor antagonist. |
| **Cyclizine** | 50 mg orally / IM / IV every 8 hours.<br>In elderly use 25 mg. | Acts on vomiting centre.<br>Histamine (H1) receptor antagonist. |
| [1]**Ondansetron** | 4 mg IV every 8 hours. | $5HT_3$ receptor antagonist. |
| [2]**Dexamethasone** | 4 mg IV / IM single dose. | Unknown |
| [3]**Droperidol** | IV dose varies – see BNF | Mainly dopaminergic receptor antagonist in chemoreceptor trigger zone. |

[1]See local policies for when to use ondansetron. No dose adjustment in the elderly is needed.

[2]Dexamethasone, is restricted for use by the acute pain team or on-call anaesthetist. It is not currently licensed for PONV. It can produce intense rectal pain when given IV to awake patients.

[3]Droperidol is restricted to use by consultant anaesthetists as a third-line antiemetic for PONV in patients unresponsive to other agents.

## General notes

- Prochlorperazine is usually used first line, however, it can cause extrapyramidal side effects and may not be the best first choice in certain patients. Seek senior advice.
- Cyclizine may be used first line, however it is not appropriate for patients with severe heart failure.
- If, after regular routine observation and assessment, it is apparent that one antiemetic is ineffective add in another. Use one which acts by a different mechanism as a combination of two antiemetic drugs acting at different sites may be more effective in resistant PONV (see table above).
- If not possible to stop opioid analgesia, consider change of opioid, and remember to prescribe simple analgesics and NSAIDs where possible.

**Continues on next page**

**Drug therapy continued**

- For choice of antiemetic in breastfeeding or pregnant women contact your clinical pharmacist for advice or Medicines Information department (Appendix 6 for contact details).
- In elderly patients (> 70 years) use lower doses of prochlorperazine and cyclizine (see table on previous page).
- Intractable vomiting may have a surgical / other serious underlying cause. Senior review is recommended.

## Other information

- ***Metoclopramide is ineffective as an antiemetic for PONV*** in licensed dosage and **should not be prescribed** as a routine antiemetic unless gastric stasis is the cause of the nausea. Restrict use in young adults under 20 years (especially women) to certain circumstances because of the risk of extrapyramidal side effects. Seek senior / specialist advice if necessary.

  Metoclopramide is contraindicated in gastrointestinal obstruction and should be avoided post gastrointestinal surgery.

# Management of Acutely Disturbed Patients, including Delirium

This guideline outlines the management of acutely disturbed patients and includes brief guidance on delirium and highlights the special considerations in elderly patients. *More detailed information on the diagnosis, prevention and treatment of delirium can be found on StaffNet.*

This guideline does not cover the management of acutely disturbed young people or adolescents. Instead contact your local adolescent psychiatry liaison for young people or adolescents for advice.

## Introduction

Most violent, aggressive or bizarre patients in general hospital wards or A&E departments are not mentally ill. Many have delirium caused by an acute physical illness and may be seriously unwell. A very small number have nothing wrong with them and should, once serious illness is excluded, be managed according to local policy for Management of Violence and Aggression.

- Causes of confusion or coma may include:
  - **T .....***Trauma, temperature*
  - **I .....***Infection*
  - **P .....***Psychiatric*
  - **S .....***Space occupying lesion, subarachnoid haemorrhage, shock*
  - **A .....***Alcohol and other drugs*
  - **E .....***Endocrine, exocrine, electrolytes*
  - **I .....***Insulin (diabetes)*
  - **O .....***Oxygen (lack of), opiates*
  - **U .....***Uraemia*
- Head injury *Refer to senior staff immediately and see head injury guideline page 186.*
- If acute alcohol withdrawal suspected see alcohol withdrawal guideline, page 173, but exclude other serious problems first!

### Signs and symptoms of delirium:

- Recent change (hours / days) in cognition, behaviour or other mental function.
- History of change from relatives / GP letter / ward staff.
- May be withdrawn ('hypoactive delirium') / unresponsive / drowsy.
- May be agitated, uncooperative, suspicious ('hyperactive delirium').
- Common if age > 65 years and acute illness / surgery / change in drugs / pre-existing cognitive impairment or dementia.

Further information on preventing and diagnosing delirium on StaffNet.

## Assessment / monitoring

- Consider delirium – see above
- Basic observation: RR, oxygen saturation ($SpO_2$), BP, temperature, blood sugar, GCS
- Check nursing notes, medical notes and observation sheets for possible causes of acute confusional states e.g. documented vital signs preceding abnormal behavior.
- Review recent drug initiation or withdrawals as cause of confusion.
- Have you excluded Hypoglycaemia, Hypoxia, Shock and Sepsis?

## Immediate non-pharmacological management

- Investigate and treat any obvious underlying cause (e.g. hypoxia).
- Correct sensory impairments and manage in a well-lit, uncluttered environment with familiar staff or relatives.
- Record duration of cognitive impairment and drug history, including alcohol and non-prescribed medications.
- Review bladder and bowels – exclude retention of urine and constipation.
- Assess and manage pain (see page 158).
- See algorithm on StaffNet for treating delirium including *verbal and non-verbal de-escalation techniques*.

## Pharmacological management **(general points to read before prescribing)**

- Emergency sedation should **always** be discussed with senior staff (STR or above). It should only be used when non-pharmacological approaches have been implemented, including verbal and non-verbal de-escalation techniques, and patient is severely distressed or is a risk of physical aggression or is a danger to themselves or others.
- Oral is preferred to parenteral therapy whenever possible.
- If drug treatment is necessary consider short-term (usually for 1 week or less) antipsychotic haloperidol **or** olanzapine (**Note**: this is an unlicensed indication for haloperidol and olanzapine).
- Start at the lowest clinically appropriate dose, titrate cautiously according to symptoms and review at least every 24 hours.
- Side effects of antipsychotics include extrapyramidal and cardiovascular side effects (including prolongation of QT interval) and rarely neuroleptic malignant syndrome.
- **Cautions / Contraindications:**
  - **Haloperidol / olanzapine –** Contraindicated in Parkinsonism and suspicion of Lewy Body dementia. Caution in patients with seizure disorders or cardiac disorders (review ECG). Haloperidol has been linked to cardiotoxicity. Haloperidol can be considered if patient's cardiac status is known and does not give cause for concern. Seek senior advice if unclear whether patient should receive haloperidol.
  - **Lorazepam –** Caution in respiratory failure, may worsen (or prolong) delirium.
- In Parkinson's Disease and dementia with Lewy bodies low dose lorazepam **may** be preferred but should be used with caution as low dose benzodiazepine can **worsen (or prolong) delirium.** Contact movement disorder specialist for advice wherever possible – low dose quetiapine may be considered by specialists.
- **Dose administration:**
  - After administering any dose, wait a **minimum of 1 hour** to judge effect and before considering repeat dosing. If there is no response after two doses, seek senior advice.
  - Do not give simultaneous injection of intramuscular olanzapine and parenteral benzodiazepine due to the potential for excessive sedation, cardiorespiratory depression and in very rare cases, death.

    If parenteral benzodiazepine is being considered, do not give until at least one hour after olanzapine IM administration.

    If the patient has received parenteral benzodiazepine, olanzapine IM administration should only be considered after careful evaluation of clinical status, and the patient should be closely monitored for excessive sedation and cardiorespiratory depression.

## Pharmacological Management – Patients with Delirium (< 65 years)

**Before prescribing** see previous page for cautions / contraindications / dose administration advice (take into account frailty when considering total daily dose)

- **Haloperidol oral 0.5 - 1 mg** or if oral not possible:

  **Haloperidol 0.5 - 1 mg initially as single IM dose (preferred route),** reassess after 1 hour and *discuss need for repeat dosing with senior staff*. **Repeat 1 - 2 mg if necessary, to maximum 5 mg.**

- **Olanzapine oral 2.5 – 5 mg (maximum combined oral / IM dose 20 mg in 24 hours).** If oral not possible:

  **Olanzapine 2.5 – 5 mg initially as a single IM dose,** reassess after 1 hour *and discuss need for repeat dosing with senior staff*. **Repeat 5 – 10 mg if necessary up to a maximum of 20 mg in 24 hours.**

  **NB:** Olanzapine IM licensed for short-term use; maximum three IM doses daily for a maximum duration of three days.

Alternative **only** if haloperidol and olanzapine are inappropriate:

- **Lorazepam oral 0.5 - 1 mg *or***

  ***Lorazepam IV 12 - 15 micrograms/kg over 2 - 3 minutes into a large vein**

  **(50 kg = 0.7 mg, 80 kg = 1.1 mg) at a maximum rate of 2 mg/minute.**

  **Or** if oral or IV not possible ***Lorazepam IM 12 - 15 micrograms/kg.**

## Pharmacological Management – Severely disturbed patients (but not elderly and no co-morbidities)

**Before prescribing** see previous page for cautions / contraindications / dose administration advice

- **Lorazepam oral 1 - 4 mg** (**N.B.** Higher oral doses may be required for patients tolerant to benzodiazepines.) **Or**

  ***Lorazepam IV 25 - 30 micrograms/kg over 2 - 3 minutes into a large vein**
  **(50 kg = 1.4 mg, 80 kg = 2.2 mg) at a maximum rate of 2 mg/minute.**

  **Or** if oral or IV not possible: ***Lorazepam IM 25 - 30 micrograms/kg**

  ***Or** (**only** if lorazepam is not available)*:

  **Diazepam (Diazemuls®) IV 2 - 5 mg into a large vein with 2 - 5 mg increments, if required, to a maximum of 10 mg (maximum rate 5 mg/minute).**

- **Haloperidol oral 1.5 - 3 mg or** if oral not possible:

  **Haloperidol IM 2 - 10 mg IM to a maximum total dose of 18 mg in 24 hours**

***Lorazapam IV / IM**: Previously there have been supply issues with IV lorazepam – seek advice from pharmacy if unable to obtain. When given by IM injection it should always be diluted 1:1 immediately before administration with water for injection or sodium chloride 0.9% as it is quite viscid when taken out of the fridge.

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## Pharmacological Management – Acutely disturbed / Delirium in elderly (> 65 years)

**Before prescribing** see page 168 for cautions / contraindications / dose administration advice

- **Haloperidol oral 0.5 - 1 mg or** if oral not possible **then give IM or**
- **Olanzapine oral 2.5 mg or** if oral not possible **then give IM or**
- ***Lorazepam oral 0.5 - 1 mg or** if oral not possible **then give IM,** see dosing advice under delirium on the previous page
- *IV sedation should not be used in elderly patients.*

***Lorazapam IV / IM**: Previously there have been supply issues with IV lorazepam – seek advice from pharmacy if unable to obtain. When given by IM injection it should always be diluted 1:1 immediately before administration with water for injection or sodium chloride 0.9% as it is quite viscid when taken out of the fridge.

## Important information

- Intensive nursing observation is mandatory after parenteral lorazepam or diazepam. ***Monitor closely for respiratory depression and have full resuscitative facilities, including high flow oxygen, suction, monitor / defibrillator and flumazenil, available***. Ensure presence of staff able to maintain a clear airway and perform basic resuscitation if necessary.
- Vital signs with HR, RR, $SpO_2$ and conscious level (AVPU or GCS) must be recorded at least hourly after emergency sedation or until senior medical review.
- Summon ward STR (or above) if no response to verbal stimulus.
- Contact duty ITU registrar immediately if any of the following occur:
  - Airway problem
  - Respiratory irregularity, RR < 10 breaths/minute or > 30 breaths/minute or $SpO_2$ < 90%
  - Acute and sustained hypotension (SBP < 90 mmHg).
- Gag reflex is not reliable as a measure of a safe airway.
- Once the acute situation has been stabilised, perform more detailed clinical assessment to identify potential underlying causes.

## Patient Consent

If patient is unable to give consent then section 47 of the Adults with Incapacity (Scotland) Act 2000 must be used (see appendix 4 for details).

- Always document in medical case record reasons for prescribing sedation, indicating review dates.
- Emergency sedation can be given under common law i.e. patient does not need to be detained (see Appendix 4 for more details). More routine sedation however requires consideration of the patient's capacity to consent. Psychiatric services can advise on the use of legislation in this regard (see Appendix 6 for contact details).

# Guidance on Night Sedation

## Patients on night sedation prior to admission

- Enquire whether the patient is a regular or occasional user of night sedation
- Continue prescription if appropriate

## Patients who have not received night sedation before

- Routine prescribing of night sedation is undesirable.
- Consider rectifiable causes of insomnia e.g. depression, pain, drugs (e.g. decongestants, theophylline, steroids or selective serotonin reuptake inhibitors (SSRIs) late in the day).
- Discuss advantages and disadvantages of night sedation with patient.
- Prescribe:

  **zopiclone 3.75 - 7.5 mg at night, preferably in the 'once only' part of the prescription form – see cautions below.**
- If prescribing zopiclone regularly, review daily and stop after the shortest possible time.

## Discharge procedure

Pharmacy **will not** supply any drug prescribed for night sedation at discharge, unless it is prescribed for a fixed interval **and** an acceptable reason for this is given in the comments section of the prescription. Contact your clinical pharmacist or dispensary for further advice (see Appendix 6 for contact details).

## Cautions

**(Refer to BNF / summary of product characteristics for full prescribing information)**

Hypnotics should be used with extreme caution in patients:

- With respiratory disease
- With a history of drug / alcohol abuse
- Who have been co-prescribed other CNS depressants
- Who are elderly or debilitated and/or have hepatic and renal impairment.

If required, a very small dose of a short-acting agent e.g. **zopiclone oral 3.75 mg at night or temazepam oral 5 mg at night** is safest in these patients.

- Hypnotics are contraindicated in severe respiratory depression and severe hepatic insufficiency.

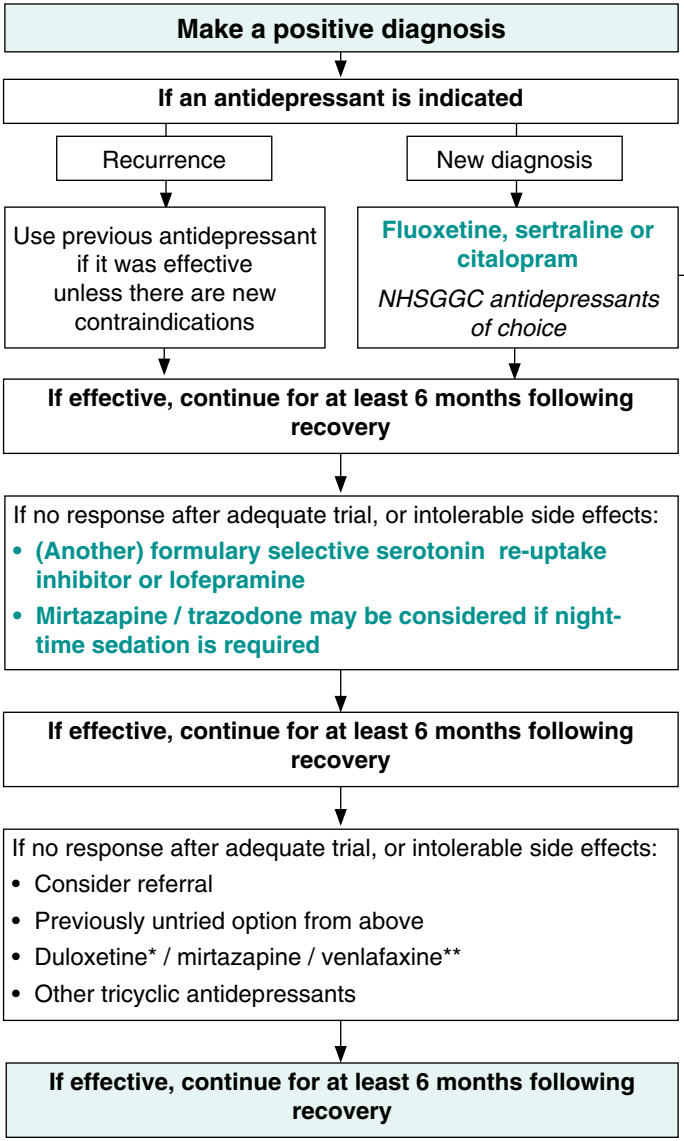
Abrupt withdrawal of benzodiazepines may cause confusion, toxic psychosis, convulsions.

## Notes

Due to the potential for dependence, there may be important legal implications for the prescriber if a patient who has been prescribed night sedation while in hospital is discharged on the drug long-term.

# Management of Depression

**N.B.** MHRA has issued dose recommendations for citalopram due to risk of a dose-dependent QT interval prolongation. The maximum dose is 40 mg/day in adults and 20 mg/day in the > 65 years and people with reduced hepatic function. See www.mhra.gov.uk for more information on cautions and contraindications.




- If mild depression, antidepressant is not indicated (NICE CG23, Management of Depression in Primary and Secondary Care, December 2004).
- Consider referral if there is a risk of suicide or the depression is severe (including psychotic symptoms).

- Safety in overdose.
- Lower potential for withdrawal effects.
- As effective as other anti-depressants.
- More cost-effective.
- Citalopram is contraindicated in patients with QT interval prolongation and in combination with drugs known to prolong QT interval. Also see note above.

- If patient is very anxious or agitated, consider the use of benzodiazepines as an adjunct for a maximum of 2 weeks.
- Agitation may be a side effect of antidepressant treatment and usually resolves after a few weeks.

*Psychiatrist initiation only.
**Regular monitoring of BP as clinically appropriate. Psychiatric supervision required for patients of daily doses of venlafaxine 300 mg and above and on initiation of a severely depressed patient.

# Management of Alcohol Withdrawal Syndrome

## Assessment / monitoring

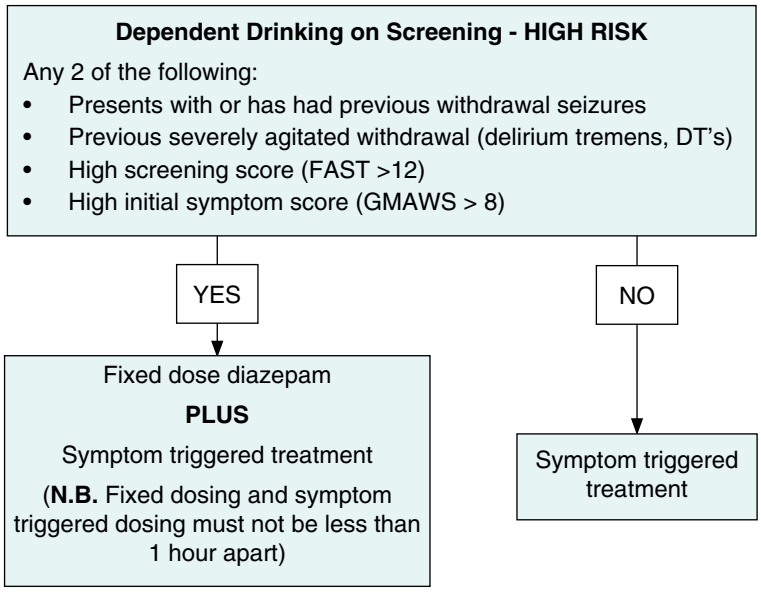
The likelihood of withdrawal reaction is indicated from a patient's history. Use the alcohol misuse assessment form to establish patient's alcohol consumption and to calculate FAST (Fast Alcohol Screening Tool) score. This will guide what initial intervention is required e.g. advice only, leaflets, referral to addiction liaison, drug intervention.

Use the flowchart below to assess whether patient is at high risk of withdrawal or not. The Glasgow Modified Alcohol Withdrawal Scale (GMAWS) sheet can be found on:

StaffNet, Clinical Guidelines Electronic Resource Directory and search for 'Alcohol'

If patient is a chronic alcohol misuser or has hazardous / harmful alcohol intake then also assess for risk of Wernicke's encephalopathy (see page 176).

**Flowchart 1: Management of Alcohol withdrawal**




## General management

For patients at high risk of alcohol withdrawal see next page for fixed dose diazepam treatment regime. There may be certain groups of patients in whom an alternative choice or route of benzodiazepine should be considered (see the next page for further information).

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### Baseline treatment regimen

- For patients at high risk of alcohol withdrawal give a fixed dose of diazepam. In the initial 24 hours prescribe:

  **Diazepam oral 20 mg 6 hourly**. If no additional symptom triggered treatment, *then reduce as follows*:

  **diazepam oral 15 mg 6 hourly for 24 hours then**

  **10 mg 6 hourly for 24 hours then**

  **5 mg 6 hourly for 24 hours then**

  **5 mg 12 hourly for 24 hours**

  For patients unable to tolerate diazepam via the oral route or presenting with severe alcohol withdrawal, see guidance below and on next page.
- Review diazepam dose if patient is excessively drowsy.
- Request senior medical review if more than 120 mg diazepam in 24 hours is given. Diazepam 120 mg is not expected to be problematic over 24 hours in uncomplicated patients.

### Exceptional patient groups

- Elderly patients
- Patients with evidence of liver disease: especially jaundice, encephalopathy.
- Patients with other significant co-morbidity (i.e. COPD, pneumonia, cerebrovascular disease, reduced GCS)

In these groups of patients consider using oral lorazepam in a symptom triggered fashion as:

**Lorazepam oral 1 - 2 mg (to a maximum of 12 mg in 24 hours before requesting senior medical review).**

**N.B.** Lorazepam has a slower onset of peak effect but ultimately a more rapid elimination.

### Severe alcohol withdrawal

These patients can exhibit aggressive / uncontrollable / dangerous behaviour. Give:

- **Diazemuls IV up to 40 mg over the first 30 minutes (max rate 2 mg/minute; flumazenil should be made available).**
  **N.B**. IV benzodiazepine should be given by experienced members of staff (FY2 or above, or nursing staff who have completed appropriate competency training on administering IV sedation).
- **Adjunctive therapy with haloperidol IV/IM 5 – 10 mg (smaller doses unlikely to be effective).**

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### Unable to tolerate oral medication

An alternative to oral diazepam or lorazepam in these patients may be IV diazemuls or lorazepam at 50% of the oral dose in the first instance (see previous page), and then assess response. Intravenous benzodiazepines should be given by experienced members of staff – see note on previous page on who can administer.

**N.B.** There are supply problems with IV lorazapam and it may not be readily available.

### Monitoring

- Closely observe for signs of over-sedation with regular observations.
- Exceptional patient groups (see previous page), patients with severe withdrawal and patients requiring IV or IM sedation require close monitoring (MEWS / SEWS), ideally with one-to-one nursing care.
- Consultation regarding intensive care support may be necessary in extreme situations.

### Other information

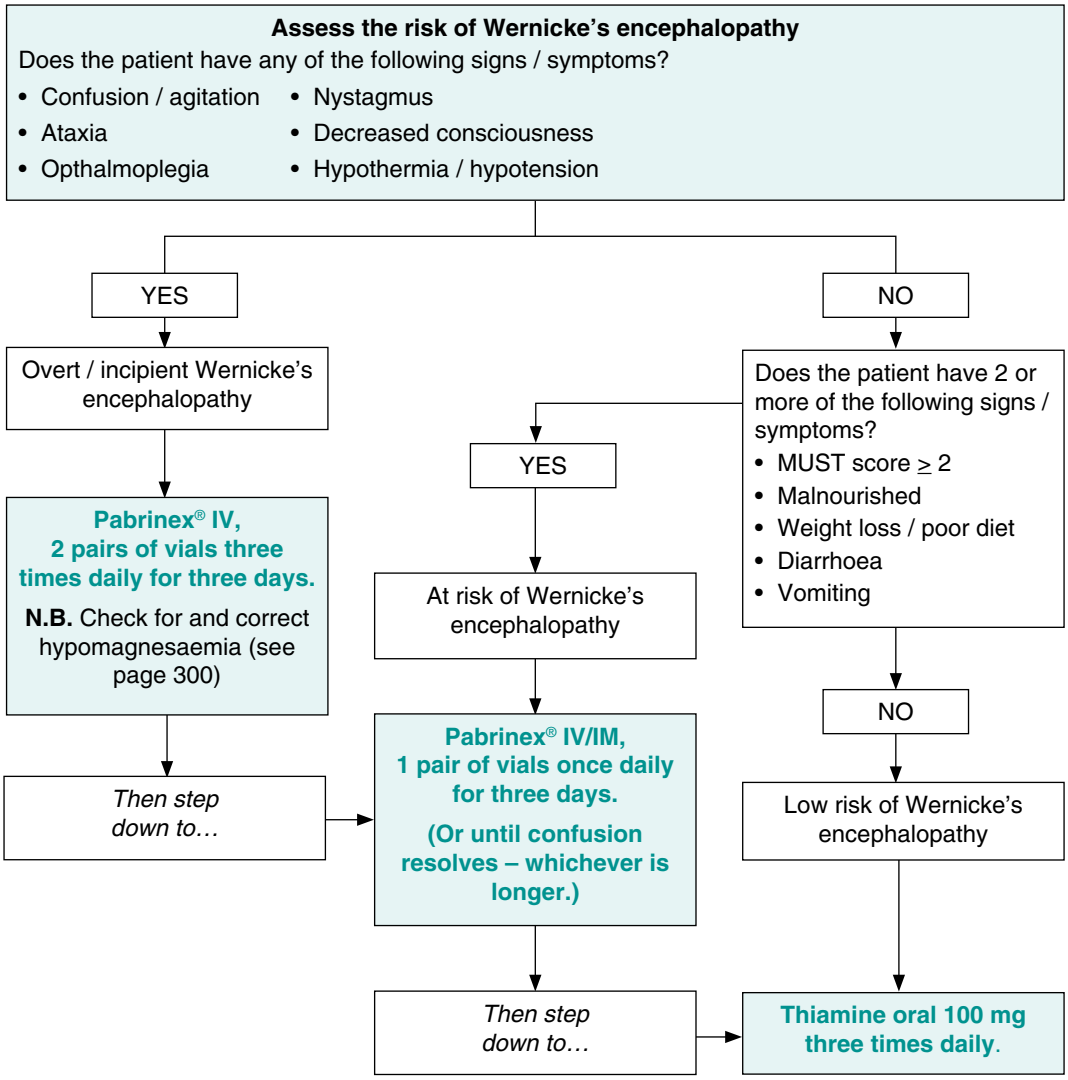
- On discharge patients should not be given regular benzodiazepine unless there is confirmed arrangement with the Community Addiction Services. Chlordiazepoxide is the recommended benzodiazepine for community use.
- Approximate oral benzodiazepine dose equivalence:

  Diazepam 10 mg = Lorazepam 1 mg = Chlordiazepoxide 30 mg

# Vitamin Prophylaxis and Treatment of Wernicke-Korsakoff Encephalopathy

## Introduction

The guidance applies to patients who are chronic alcohol abusers. This includes those who are dependent on alcohol but also those who have a hazardous / harmful alcohol intake.




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## Important notes

- Patients with overt / incipient Wernicke's encephalopathy or 'at risk' of Wernicke's encephalopathy **must** be given Pabrinex® **before** the administration of glucose or nutritional support.
- Intravenous Pabrinex® should be administered over 30 minutes.
- Anaphylaxis is a rare complication of IV Pabrinex® administration and even more uncommon with IM administration. Monitor patient for wheeze, tachycardia, breathlessness and skin rash. Facilities for the administration of adrenaline and other resuscitation should be available (see page 18 for anaphylaxis management).
- Further vitamin supplementation as clinically indicated by responsible medical team in the context of a general nutritional assessment.

# Management of Drug Misusers in Hospital

This guideline is an abbreviated version of the full guideline – Management of Drug Misusers in Glasgow and Clyde Acute Hospitals - on StaffNet, Clinical Guideline Electronic Resource Directory and primarily focuses on opiate (heroin) and benzodiazepine misuse. It is only intended as a guide and is not comprehensive. For patients with complex needs (e.g. maternity addiction, pregnant) or challenging behaviours, seek advice from specialists (see appendix 6 under 'Drug Misuse' for contact details). For patients on buprenorphine (Subutex® / Suboxone®) prescriptions, or for guidance on pain management see the full guideline on StaffNet.

## Assessment / monitoring

- Establish history of drug misuse. If appropriate and agreeable with the patient undertake clinical examination and look for signs of withdrawal (see table 1). Assess whether patient's clinical state is compatible with their declared use. Exclude other illnesses which may cause symptoms similar to opioid withdrawal.
- Send for urinalysis. Near patient testing strips will give a drug screen for the major drugs of addiction in a few minutes. If the patient declines consent for this then treatment, especially substitute prescribing, cannot be safely undertaken and will therefore not be part of the treatment plan.

**Table 1 – Subjective opioid withdrawal scale (SOWS)**

| | 2 points | 1 point | 0 points |
|---|---|---|---|
| **Pupil size** | Wide | Normal | Pin point |
| **Palms** | Wet | Moist | Dry |
| **Skin** | Goosed | Cold | Warm |
| **Nasal** | Running | Sniffing | Dry |
| **Agitation** | Can't sit | Agitated | Calm |
| **GIT** | Vomiting | Nausea | Normal |
| **Pulse** | > 100 | 80 - 100 | < 80 |
| **TOTAL** | A score of > 5 is strongly suggestive that the patient is suffering from opiate withdrawal | | |

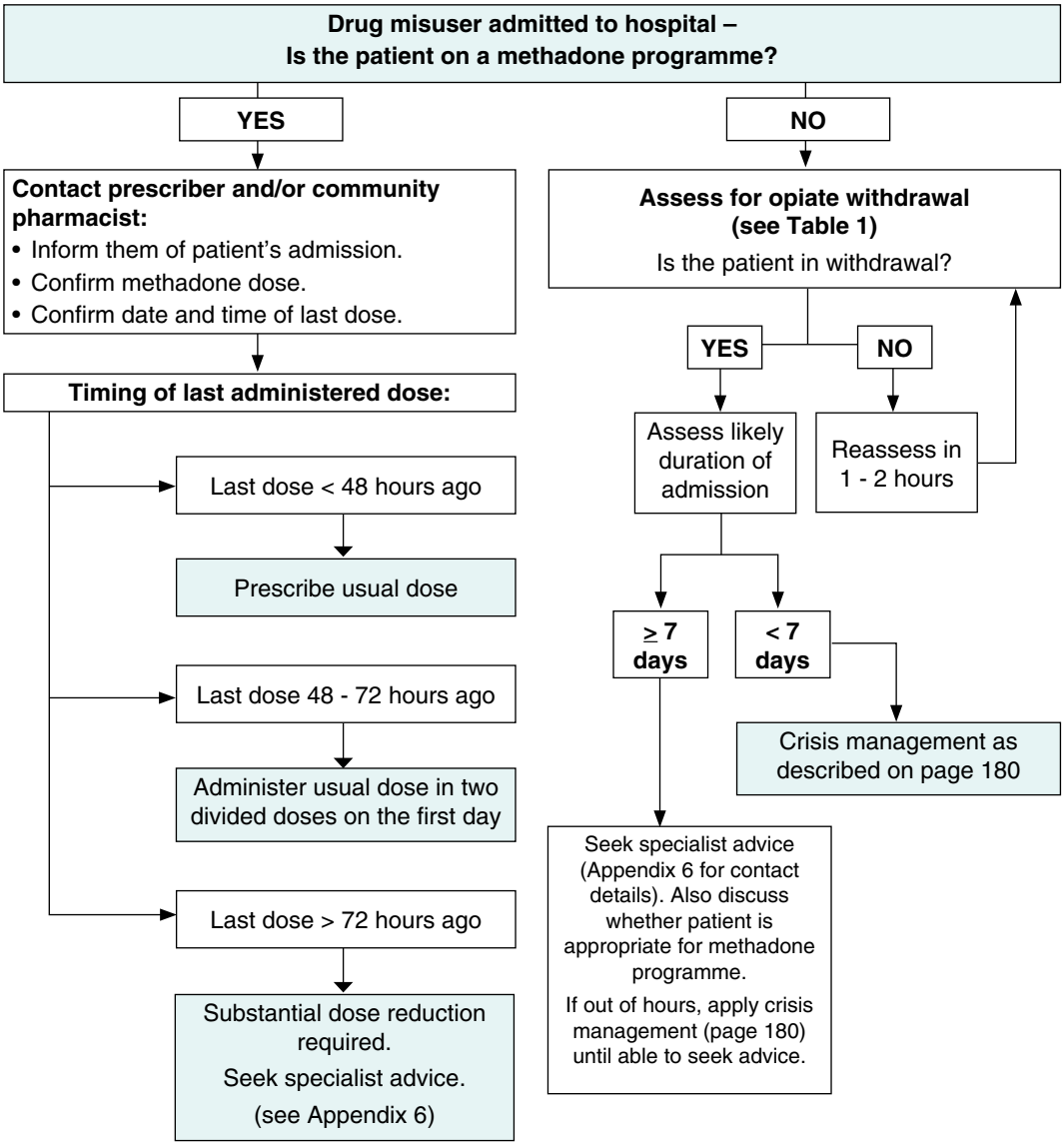
- For patients experiencing pain following injury or surgical procedure and who are on evidenced substitute prescribing see the full guideline on StaffNet.

## General management

If patient is a polydrug user **not on** treatment, presenting with withdrawal and requiring overnight admission, then crisis management regimens described under the 'Treatment Options' section on pages 180 - 182 may be appropriate.

**Do not feel pressurised to prescribe**. Only prescribe when assessment, examination and investigations have been completed and indicate that prescription is appropriate.

## Flow diagram for use with Hospital Guidelines on the Management of Opiate Misusers in Hospital



## Treatment options

(**N.B.** All these medications should be taken under supervision.)

**Exercise extra caution when prescribing methadone or benzodiazepines.**

- If patient is pregnant, always contact specialists for advice (see Appendix 6 under Drug Misuse).
- If patient is receiving opiate analgesia or other sedating medications seek advice from addictions specialists. If patient has severe pain then IV / SC morphine is the regimen of choice – avoid IM analgesics and do not use pethidine.
- If oral doses cannot be given then greatly reduced parenteral doses may be required. Seek advice from addiction specialists (Appendix 6 for contact details) as dose conversion can vary on a case by case.
- Respiratory disease present or suppressed respiratory drive. Observe RR closely.
- In liver disease / hepatitis
- Head injury as GCS will not be sensitive enough to assess opiate intoxication.
- Drug interactions. Check if effects of methadone or benzodiazepine will be altered.

## Crisis management prescribing for opiate misusers

(See flow diagram on page 179 for when to use crisis management.)

**Dihydrocodeine oral up to 60 mg four times daily (unlicensed use).**

- Dihydrocodeine can be given for the first 24 - 48 hours, but not in pregnancy (contact NHSGGC SNIPs for advice), if use of methadone is either inappropriate or there is a delay in initiating methadone because:
  - Awaiting further assessment
  - Awaiting methadone dose confirmation
  - It is a short-term admission and through care is not possible.
- Dihydrocodeine dose can be reduced or maintained during short admissions depending on the clinical condition of the patient.
- If required, incremental reductions can be daily or every other day.
- Liquid preparations are preferred to enable supervised administration.
- **Do not** supply on discharge.

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## Methadone prescribing

- For patients not on a methadone programme speak with specialist if patient is likely to be in hospital for > 7 days. If methadone is advised then table 2 outlines management for the first 3 days.
- Patients requiring > 100 mg of methadone should be monitored for prolongation of QT interval and torsades to pointes.
- Methadone has a long half-life (14 – 72 hours, mean about 24 hours). It is frequently lethal in overdose and in appropriate maintenance dose (60 mg – 120 mg) when given to patients who have lost their tolerance to opiates or opiate naïve patients.
- If patient is newly commenced on methadone and requires doses > 60 mg/day seek specialist advice (Appendix 6 for contact details, under 'Drug Misuse') before prescribing.
- Stop if any signs of intoxication e.g. drowsiness, slurred speech or respiratory depression. May need to administer naloxone IV/IM. This is contraindicated in pregnancy, however in life-threatening situation use with caution at lowest possible dose.
- On discharge do not supply methadone. Instead:
  - If discharge for short period (< 3 days) before return to hospital advise the patient to return to ward for daily supervised dose.
  - For all other patients see full guideline on StaffNet for details. Ensure continued prescription and interim continuity of care are organised in advance of patient discharge. Also ensure patient's GP or Community Addiction Team prescriber and Community Pharmacy are aware of methadone dose and time of last dose given in hospital.
- Advise patient to see GP whether or not methadone is prescribed by GP.

**Table 2 – Initial methadone oral dose**

| Day | Methadone dose |
|---|---|
| **1** | 20 mg initially. Reassess 12 hours later and give further 10 mg dose only if withdrawal effects are still evident (maximum total dose on day 1 is 30 mg) |
| **2** | Same total dose as day 1 |
| **3** | As above |

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## Crisis management prescribing for benzodiazepine misusers

There are two suggested regimens to prevent withdrawal in patients who have been taking over 40 mg diazepam or 80 mg temazepam daily.

### Option 1

**Table 3 – Suggested oral detoxification or maintenance regimen for short-term admissions for benzodiazepine misuse.**

| Diazepam oral daily dose | Regimen |
|---|---|
| 20 mg three times daily | for 3 days (Days 1-3) |
| 15 mg three times daily | for 3 days (Days 4-6) |
| 10 mg three times daily | for 3 days (Days 7-9) |
| 5 mg three times daily | for 3 days (Days 10-12) |
| 5 mg twice daily | for 3 days (Days 13-15) |
| 5 mg once daily | for 3 days (Days 16-18) |

If required, incremental reductions can be daily or every other day.

### Option 2

An alternative regimen for patients whose benzodiazepine use is uncertain or lower than described above:

**Diazepam oral 10 mg as a single dose.** Reassess patient 6 hours later and if not drowsy or intoxicated then this may be repeated 6 hourly. Reduce dose during stay.

## Benzodiazepine prescribing – general notes

- Diazepam detox should be agreed on an individual basis according to level of use and length of hospitalisation. In pregnancy always consult NHSGGC SNIPs (see Appendix 6 for contact details).
- For those misusing opiates plus benzodiazepines and/or alcohol, for whom no through care is possible, a combination of treatments outlined above can be prescribed. Please also refer to the Glasgow Modified Alcohol Withdrawal Scale (GMAWs). Further guidance in crisis management prescribing for opiate misusers is outlined in the full guideline for drug misusers in GGC acute hospitals on StaffNet.
- It is recognised that the doses of diazepam for this patient group are well above those normally prescribed.
- If sedation or intoxication is produced the dose can be withheld until clinical condition is satisfactory. Then proceed with reduced dosage.
- Do not assume if a patient becomes unusually drowsy that they have had illicit drugs. There may be an underlying medical reason that requires further investigation and patient should be closely monitored.

# Management of Suspected Subarachnoid Haemorrhage (SAH)

**(Also see SIGN 107)**

## Introduction

A patient presenting with *headache that reaches its maximum severity instantaneously or over a few minutes* should be assessed for possible SAH, unless a history of similar recurrent stereotyped events indicates an alternative diagnosis (e.g. coital headache, cough headache, severe migraine).

## Assessment / monitoring

Use the flow diagram on the next page to systematically assess the patient for SAH. CT scanning should **ideally** be done before proceeding to lumbar puncture (LP).

Differential diagnoses to consider in the case of a negative CT result include:

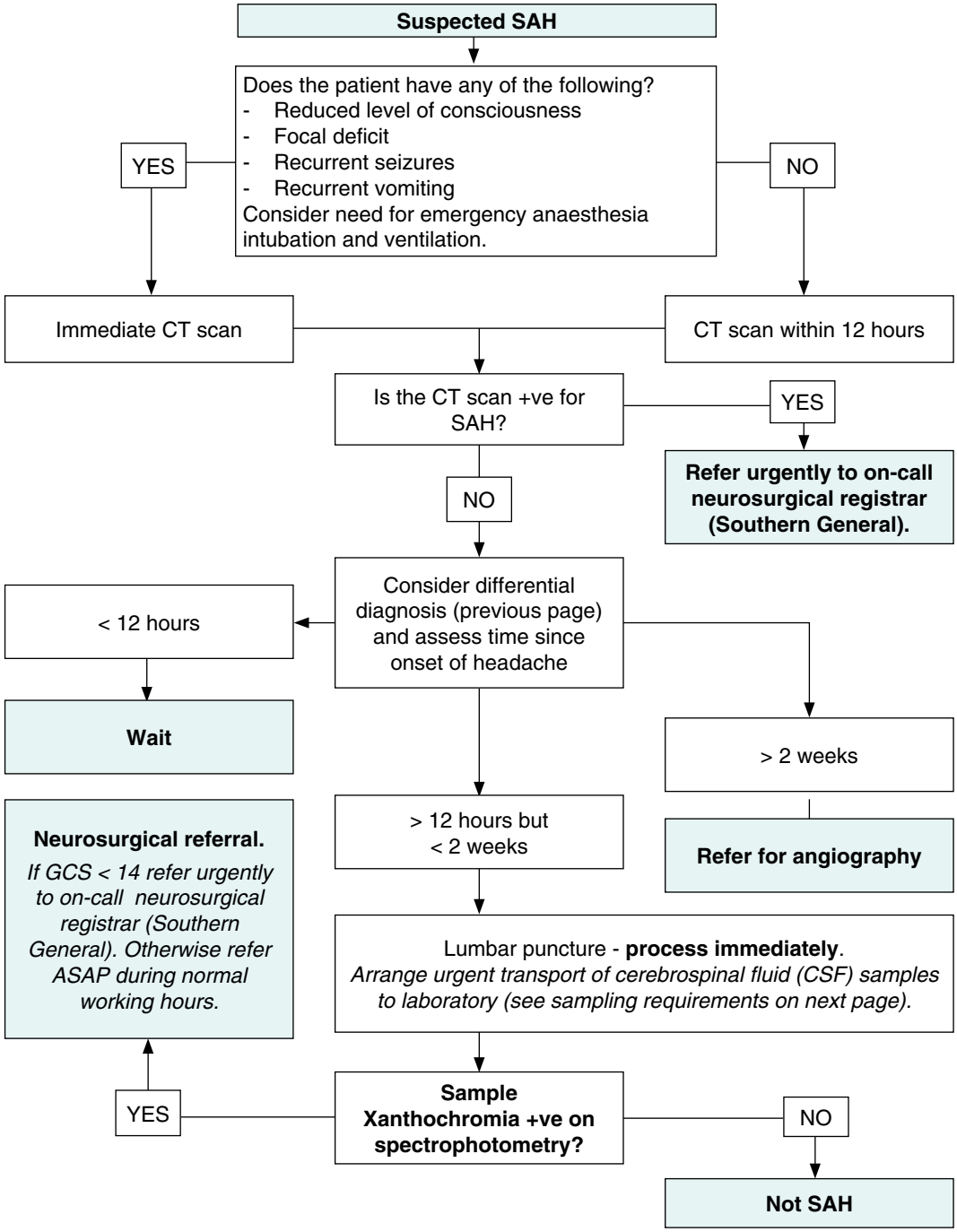
- Sagittal sinus thrombosis
- Pituitary apoplexy
- Intracranial hypertension
- Malignant hypertension
- Carotid or vertebral dissection
- Ischaemic stroke
- Migraine / cluster headache
- CNS infection

Most alternative diagnoses which require immediate management can be excluded by history, routine examination, CT and LP. However, some patients may require additional tests such as a CT venogram for patients with suspected Sagittal sinus thrombosis.

Further assessment and monitoring **in patients with confirmed SAH**:

- **A**irway, **B**reathing and **C**irculation optimised
- Monitor (2 hourly) vitals (BP, Pulse), GCS
- Urinary input / output
- FBC, U&Es (including magnesium), glucose, coagulation screen, Group and Hold
- Pregnancy screen

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**Sampling requirements for the Biochemical Investigation of SAH (CSF Xanthochromia):**

1. Spectrophotometric analysis of CSF for xanthochromia is useful in the diagnosis of SAH particularly when CT is not conclusive.
2. It is recommended that CSF is not sampled until at least 12 hours after a suspected event.
3. The CSF sample should be centrifuged within 15 minutes of sampling. Phone the laboratory to ensure a technician is available before taking the CSF sample.
4. The CSF sample for xanthochromia analysis should always be **the last fraction to be taken** and the volume of sample must be **a minimum of 1 ml**.
5. Record on the request form:
   - the clinical indication for the request
   - the time of headache onset
   - the time of LP
   - if the differential diagnosis includes meningitis.
6. Protect the CSF sample from light by placing it in a brown paper envelope.
7. Analysis is done between 9 am - 5 pm weekdays, and Saturday and Sunday mornings. The result will be phoned to the ward.

## General management

Consider Medical ward / ICU / HDU / Neurosurgical ward (after discussion with the neurosurgeon) depending on the patient's condition.

## Drug therapy / treatment options

- TED supportive stockings
- Isotonic fluids e.g.:
  **sodium chloride 0.9% IV 3 litres over 24 hours** (do not restrict fluid if hyponatraemia develops).
- Ensure adequate analgesia e.g.:
  **paracetamol +/- dihydrocodeine 50 mg IM or dihydrocodeine 30 mg orally every four to six hours.** (Avoid other opiates, NSAIDs.)
- **Nimodipine 60 mg orally or via NG tube every 4 hours for 21 days.** Once tablet is crushed for NG administration it is extremely light sensitive so must be administered immediately.
- **Ranitidine 50 mg IV three times a day or 150 mg orally twice a day as stress ulcer prophylaxis.**

**Phenytoin if necessary for seizures** (see page 192 for dosage calculations).

# Guidelines for the Management of Patients with Recent Head Injury

**(Also see SIGN 110)**

Head injuries presenting to hospital should be managed according to SIGN guidelines. Multiply injured patients with a reduced level of consciousness should be managed by experienced staff using principles of Advanced Trauma Life Support. A reduced level of consciousness must not be assumed to be due to drug or alcohol intoxication in a patient with a history or examination findings consistent with a head injury.

## Indications for admission to a hospital ward

**Patient has:**

- Impaired level of consciousness (GCS < 15/15).
- Is fully conscious (GCS 15/15) but has any indication for a CT scan (patient can be considered for discharge if CT scan is normal and there are no other reasons for admission).
- Significant existing medical problems e.g. anticoagulant use.
- Social problems or cannot be supervised by a responsible adult.

## Indications for discharge

Patient can be discharged from A&E for observation at home if fully conscious (GCS 15/15) with no additional risk factors or other relevant adverse medical and social factors.

**Prior to discharge the following criteria must be met:**

- A responsible adult is available and willing to observe the patient for at least 24 hours.
- Verbal and written instructions about observations to be made and action to be taken are given to and discussed with that adult.
- There is easy access to a telephone.
- The patient is within reasonable access of medical care.
- Transport home is available.

## Referral to Neurosurgical Unit

**Refer if:**

- Persisting coma (GCS score $\leq$ 8/15) after initial resuscitation.
- Confusion which persists for more than four hours.
- Deterioration in level of consciousness after admission (a sustained drop of one point on the motor or verbal subscales, or two points on the eye opening subscale of the GCS).

*Continues on next page*

*Referral to Neurosurgical Unit continued*

- Focal neurological signs.
- A seizure without full recovery.
- Compound depressed skull fracture.
- Definite or suspected penetrating injury.
- A CSF leak or other sign of a basal fracture.

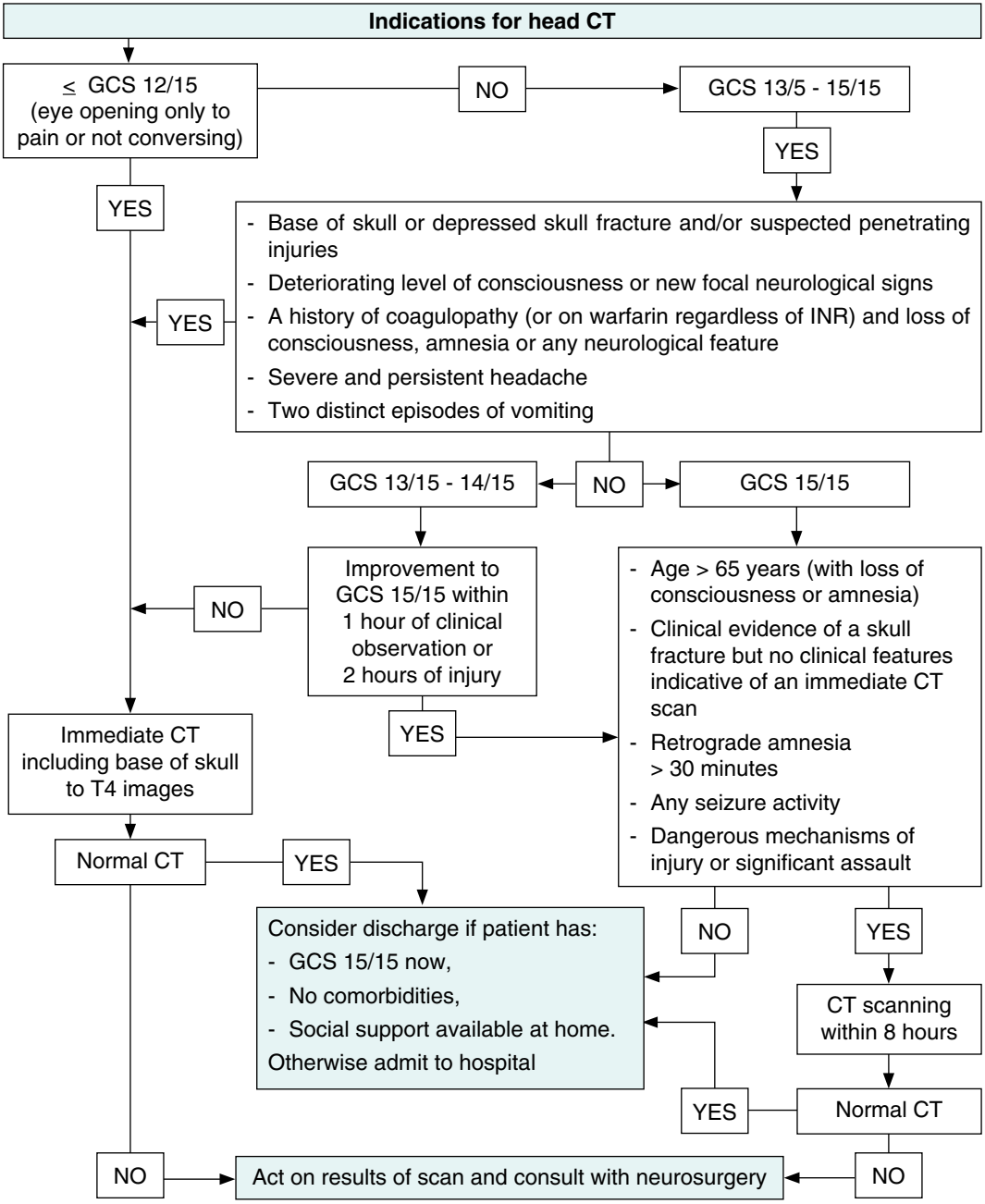
## Indications for imaging in head injuries

- Where CT is available, skull x-rays should not be performed.
- In adults with GCS < 15/15, with indications for a head scan, CT of the cervical spine should also be performed down to body of T4.

**See flow chart on next page for indications for head CT.**

*Continues on next page*

SIGN 110. Early management of adult patients with a head injury. Quick Reference Guide (May 2009). Algorithm adapted with permission.



# Management of Status Epilepticus

## Introduction

Tonic-clonic status epilepticus (continuing or recurrent seizures over 30 minutes, or without recovery) is a medical emergency with a 10 - 15% mortality rate. There is a risk that seizures will cause cerebral damage if not controlled within 30 minutes of onset.

Pre-status epilepticus is a phase of accelerating seizures which usually takes place prior to the development of frank status epilepticus. Status epilepticus can be avoided if treatment is given at this stage.

This guideline outlines the general management of tonic-clonic status epilepticus in adults and is based on the SIGN guideline for diagnosis and management of epilepsy in adults. Treatment may differ in individual clinical circumstances

## Assessment / monitoring

See flow chart on next page for general assessment and monitoring. Treatment should not be delayed. Note timings throughout in order to assess when to escalate treatment. Assess patient for possible causes such as:

- Poor compliance with Anti-Epileptic Drugs (AEDs), change of drug therapy, drug interactions.
- Infection
- Acute cerebral insult (encephalitis, meningitis, trauma)
- Cerebral tumour (often frontal lobe)
- Drug overdose (e.g. antidepressants)
- Drug withdrawal (e.g. alcohol, benzodiazepines etc.)
- Pseudostatus should be considered. If blood gases are normal or suggest hyperventilation, despite apparent prolonged major seizures then pseudostatus is likely. Diagnosis is aided by EEG. Get neurological advice before proceeding to general anaesthesia and ITU.

## Management of Status Epilepticus / Pre-status Epilepticus

Prevention: Carers should treat serial or prolonged seizures in the community with rectal diazepam or intranasal / buccal midazolam according to an agreed protocol (protocol must include advice on when to transfer to hospital).

***For status epilepticus*** see flow chart on next page for management. Do not delay treatment.

***For pre-status epilepticus***, do not delay treatment. Give lorazepam IV or diazepam rectally as per flowchart. AED treatment needs to be restored / maintained as quickly as possible. If in doubt about compliance give one complete dose of all usual AEDs. If no information on previous treatment or seizures continue to accelerate, proceed to additional AED treatment (as per status epilepticus guideline).

***For both status epilepticus and pre-status epilepticus*** assess aetiology and correct if possible.

*Continues on next page*

# Patients with generalised tonic-clonic status epilepticus

Adapted with permission from SIGN 70: Diagnosis and Management of Epilepsy in Adults. A national clinical guideline (April 2003).

***Immediate measures***

- Open and maintain airway.
- Give oxygen.
- Assess cardiac and respiratory function.
- Secure intravenous (IV) access in large veins.
- Collect blood for bedside blood glucose monitoring and FBC, U&Es, LFTs, calcium, glucose, clotting, AED levels and store for later analyses.
- Measure blood gases to assess extent of acidosis.

↓

**Give lorazepam IV up to 4 mg (e.g. 2 mg over 1 minute, may be repeated after 3 - 5 minutes) or if lorazepam is unavailable, give diazepam IV up to 10 mg**

↓

No response?

↓

Repeat after maximum of 10 minutes if in hospital.

Delay in gaining IV access in community.

↓

Give **10 - 20 mg diazepam rectally.**

Determine aetiology:

- Any suggestion of hypoglycaemia: give **50ml of 50% glucose IV.**
- Any suggestion of alcohol abuse or impaired nutritional status: give **thiamine IV (as 2 pairs of Pabrinex® ampoules).**
- **Give usual AED treatment** - can be given by nasogastric tube if airway secured (or IV if necessary for phenytoin, sodium valproate and phenobarbital).

↓

***Within 30 minutes***

If status persists

↓

- Give **phenytoin IV 18 mg/kg*, at a rate of 50 mg/minute or less; with ECG monitoring**
  *Dose recommended higher than licensed dose but based on SIGN recommendations. ***Refer to page 192 for further phenytoin dosing information.***
- Call ITU to inform of patient.

↓

***> 30 minutes***

If status persists

↓

- Administer general anaesthesia and admit to ITU.
- Monitor using EEG to assess seizure control.
- Refer for specialist advice.

# Other

## Initiating Long-term Anti-epileptic Drugs

In status epilepticus, immediate treatment is required to reduce the risk of cerebral damage. Once seizures are controlled, consideration should be given to long-term anti-epileptic treatment. Recommendations on appropriate therapy should be sought from an epilepsy specialist, however the patient should not be left untreated while waiting for specialist advice.

Patients who **do not** present with status epilepticus but who require long-term anti-epileptic drugs should be referred to an epilepsy specialist / neurologist (usually outpatient service) and ideally no medication should be started in the meantime. (SIGN Guideline Number 70 recommends that in epilepsy, treatment should only be initiated by a specialist.) For elderly patients current practice of management by a physician specialising in medicine for the elderly should continue, with specialist neurological advice available when necessary.

Generally long-term anti-epileptic therapy is not usually indicated in patients:

- If the cause of the seizures is known and can either be withdrawn or corrected or
- As prophylaxis therapy following an acute brain injury.

# Guideline for Phenytoin Dose Calculations

## 1. Initial loading dose of phenytoin for status epilepticus

If the patient has not already received phenytoin then give:

**Phenytoin sodium IV 18 mg/kg** (see Table 1).

*Ensure ECG, blood pressure and respiratory function are monitored throughout the duration of the infusion.*

**Table 1 – IV phenytoin loading dose**

| Weight (kg) | IV Loading Dose (mg) | Volume of IV phenytoin (ml) (vial = 250 mg/5ml) |
|---|---|---|
| 35 - 44 | 700 | 14 |
| 45 - 54 | 900 | 18 |
| 55 - 64 | 1100 | 22 |
| 65 - 74 | 1250 | 25 |
| 75 - 84 | 1450 | 29 |
| 85 - 94 | 1600 | 32 |
| > 94 | 1800 | 36 |

### Phenytoin IV administration

- Give phenytoin over 30 - 40 minutes (rate < 50 mg/minute). In patients who are elderly, or have pre-existing cardiac disease, give phenytoin over 60 - 80 minutes (rate < 25 mg/minute).
- Ideally, administer undiluted via a syringe pump through a large gauge needle or IV catheter into a large forearm vein.
- If dilution is essential, mix with 100 - 250 ml sodium chloride 0.9% to a final concentration of < 10 mg/ml, and administer by infusion pump.
- Use the solution immediately, ideally with a 0.2 - 0.5 micron in-line filter.
- To avoid local venous irritation, inject sterile sodium chloride 0.9% through the vein or catheter before and after each phenytoin infusion.
- **Do not** administer as a continuous infusion.

**Phenytoin 'Top-up' loading dose continues on next page**

Continued from previous page

## 2. 'Top-up' loading dose of phenytoin for status epilepticus

If phenytoin is already present but the patient is still not controlled, a 'top-up' loading dose may be useful.

**Phenytoin sodium 'top-up' dose (mg) = (20 - measured concentration (mg/L)) x 0.7 x wt (kg)**

Table 2 gives the approximate increase in concentration following doses of 250 – 750 mg. For example, if the patient weighs 70 kg and has a measured concentration of 5 mg/L, a single dose of 750 mg will increase the concentration to around 20 mg/L (5 mg/L + 15 mg/L).

**Table 2 – Increase in phenytoin concentration with 'top-up' doses**

| | Concentration increase with 'top-up' dose | | | |
|---|---|---|---|---|
| Weight / Dose | **50 kg** | **60 kg** | **70 kg** | **80 kg** |
| **250 mg** | 7 mg/L | 6 mg/L | 5 mg/L | 4.5 mg/L |
| **500 mg** | 14 mg/L | 12 mg/L | 10 mg/L | 9 mg/L |
| **750 mg** | 21 mg/L | 18 mg/L | 15 mg/L | 13.5 mg/L |

## 3. Maintenance dose of phenytoin

**Phenytoin typical doses are 3 - 5 mg/kg/day. The first dose should be given 12 - 24 hours after the loading dose.**

Oral or nasogastric administration should be used, whenever possible. Only use intravenous administration when these options are not feasible and where cardiac monitoring is available.

### Notes

- Phenytoin sodium 100 mg capsules / tablets / injection = 15 ml (90 mg) suspension (6 mg/ml).
- There are many drug interactions with phenytoin (consult the BNF Appendix 1 or your clinical pharmacist).
- Phenytoin concentrations increase disproportionately with dose; toxicity may occur if the maintenance dose is increased by more than 25 - 50 mg per day. Table 3 on the next page may help with dosage adjustment. Based on the patient's current dose and the measured concentration (columns 1 and 2), column 3 gives a rough guide to interpretation of the result and possible dosage adjustment.

**N.B.** Table 3 is for maintenance dose adjustment only. For 'top-up' doses in urgent situations see Table 2.

*Continues on next page*

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**N.B.** Table 3 is for phenytoin maintenance dose adjustment only. For phenytoin 'top-up' doses in urgent situations see Table 2 on previous page.

**Table 3 – Phenytoin maintenance dose adjustment**

| Measured concentration | Current dose | Maximum dose increase |
|---|---|---|
| < 5 mg/L | < 4.5 mg/kg/day | 100 mg |
| | 4.5 - 6 mg/kg/day | Check compliance |
| 5 - 10 mg/L | 4.5 - 6 mg/kg/day | 50 mg |
| | > 6 mg/kg/day | Check compliance |
| 10 - 20 mg/L | - | 25 mg |

# 4. Therapeutic Drug Monitoring of Phenytoin

**Target concentration range: 5 - 20 mg/L**

### Routine monitoring during maintenance therapy

- Trough concentration (i.e. sample prior to next dose)
- Sample 3 - 5 days after starting a maintenance dose or following a dose change
- Re-analyse 5 - 10 days later as further accumulation may occur

### Monitoring after a loading / top-up dose

- 2 - 4 hours after an IV dose or 12 - 24 hours after an oral dose or according to clinical response.
- Daily monitoring may be necessary until control is achieved and concentrations stabilise.

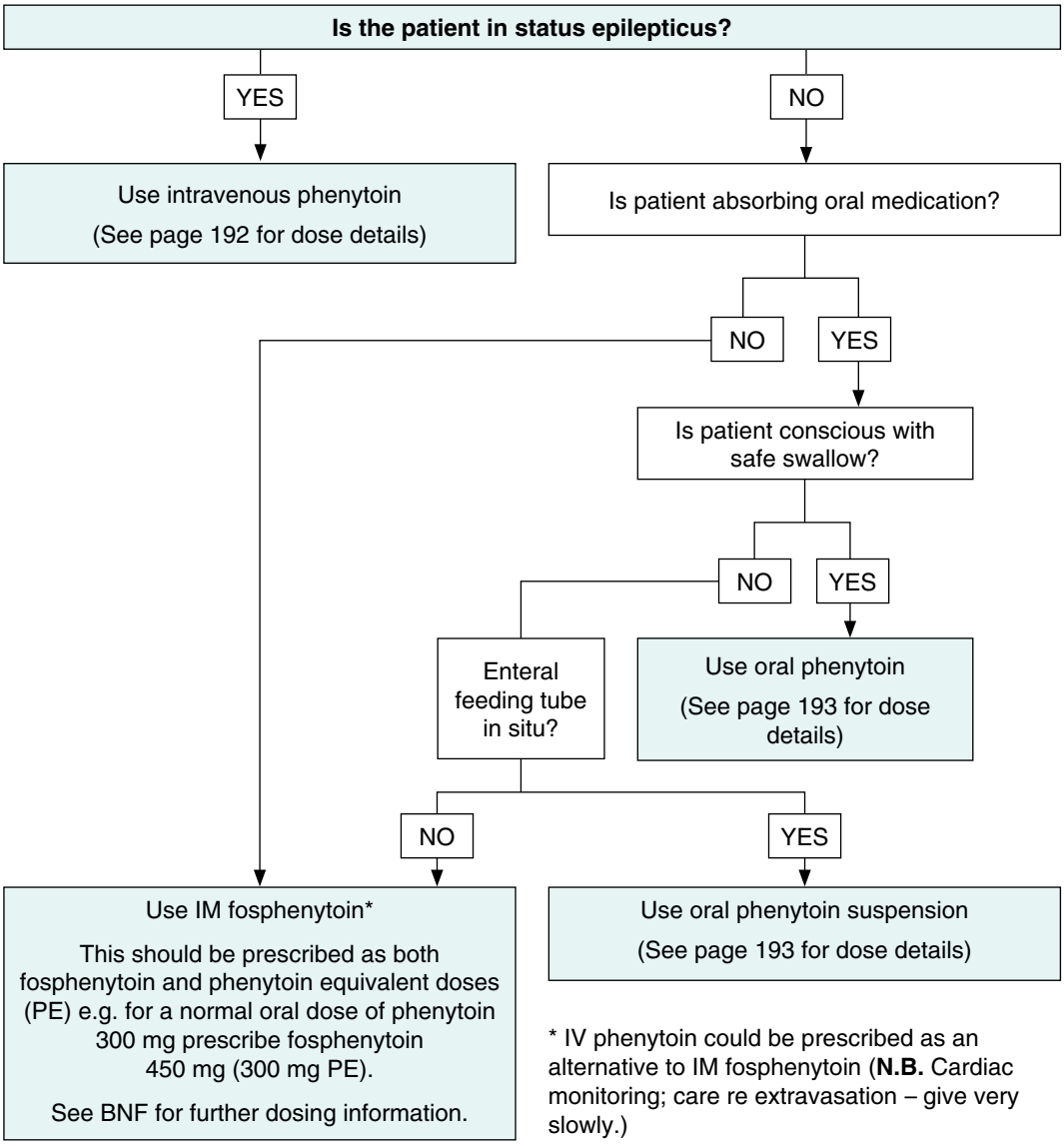
### Notes

- The patient's clinical status is more important than the concentration measurement.
- The interpretation of concentration measurements is altered in:
  - hypoalbuminaemia (especially < 32 g/L),
  - uraemia
  - pregnancy

*Seek advice from biochemistry or your clinical pharmacist.*

*Continues on next page*

## Decision making algorithm for the administration of phenytoin formulations




* IV phenytoin could be prescribed as an alternative to IM fosphenytoin (**N.B.** Cardiac monitoring; care re extravasation – give very slowly.)

# Parkinson's Disease in Acute Care

## Introduction

This guidance highlights the importance of continuing Parkinson's disease (PD) medication and covers the first-line management of PD patients who have:

- Nil by mouth status
- Confusion / hallucination / agitation
- Dizziness and falls
- Nausea and vomiting

## Assessment / monitoring

It is **crucial not to stop PD drugs** for any significant length of time i.e. > 2 hours or to miss any doses as there is a risk of Neuroleptic Malignant-Like Syndrome (Parkinson hyperpyrexia syndrome, PHS) which may be fatal. Symptoms include rigidity, pyrexia, and reduced conscious level. There may be features of autonomic instability, and serum creatine kinase (CK) may be elevated. Complications of PHS include acute renal failure, aspiration pneumonia, deep venous thrombosis / pulmonary embolism and disseminated intravascular coagulation.

## General management

Where a patient does not have an individual supply of their PD medication, access supplies via the pharmacy or the local main holding areas of PD medications across NHSGGC A full list of the PD medicines available in holding areas across NHSGGC sites is available on StaffNet, Clinical guideline electronic resource directory, search for "NHSGGC Parkinson's disease PD medication stock list across acute hospitals".

It is important for PD medications to be administered at exact times. This should be clearly annotated on the prescription chart.

### Table 1 - Location of PD medicines across acute hospital sites

| Site | Location |
|---|---|
| Gartnavel General Hospital | Ward 3A |
| Glasgow Royal Infirmary | Ward 18/19 |
| Inverclyde Royal Hospital | Ward 2 |
| Royal Alexandra Hospital | Ward 5 |
| Southern General Hospital | Ward 57 |
| Victoria Infirmary | Ward 15 / MHU – Ward North 2 |
| Vale of Leven | Ward 14 |
| Western Infirmary | Emergency Drug Cupboard |

Inform PD nurse specialist of all PD patient admissions (see Appendix 6 for contact details)

*Continues on next page*

# Drug therapy / treatment options

## Nil by mouth patients

Seek advice from a clinical pharmacist, Medicines Information (see Appendix 6 for contact details), Parkinson's disease nurse specialist or on-call pharmacist (out of hours) regarding alternative formulations.

## Confusion / hallucination / agitation

- Only if necessary treat with benzodiazepine.
- **Avoid** first generation antipsychotics e.g. haloperidol or chlorpromazine.
- Refer to Management of Acutely Disturbed Patients, including Delirium - page 167.
- Refer to PD specialist for assessment as soon as possible.

## Dizziness and falls

- Review need for drugs which precipitate postural hypotension or affect cardiac function e.g. anti-hypertensives, heart failure drugs, tricyclic antidepressants, anticholinergics, acetylcholinesterase inhibitors.
- PD medications and PD itself may be associated with orthostatic hypotension (check standing BP).
- Refer to PD specialist for assessment as soon as possible.

## Nausea and Vomiting

- Use domperidone either orally or rectally (if necessary). Use the lowest effective dose. See BNF for further dosing advice.*

  **Caution**: domperidone may prolong QT interval. *Risk of QT interval prolongation may be higher in patients older than 60 years and at daily doses of more than 30 mg. Avoid prescribing domperidone with other QT interval prolonging drugs (see www.qtdrugs.org for further details). Consider alternatives in at risk patients.
- **Cyclizine oral/IM/IV 50 mg every 8 hours (in elderly use 25 mg)** or ondansetron (unlicensed use) are also appropriate.

  **Note**: Ondansetron may prolong QT interval, use with caution.
- **Avoid** metoclopramide and prochlorperazine.

## Subcutaneous Apomorphine (for infusion)

- All patients admitted to hospital on apomorphine should be referred to the PD nurse specialist, movement disorders team or pharmacist for advice as soon as possible (see appendix 6 for contact details).
- An NHSGGC monograph for maintaining apomorphine subcutaneous infusion treatment in patients admitted to hospital is available on StaffNet.
- Apomorphine should only be instigated with the guidance of a prescriber experienced in PD (it is not suitable for emergency administration in a drug naïve patient). If a patient is already established on this then it must be continued.

Section 7

# Infections

# Management of infections

## Introduction

Appropriate and prudent use of antimicrobials is important as misuse of these agents is associated with treatment failure, antibiotic resistance, healthcare associated infections (including *Clostridium difficile* and MRSA) and increasing cost. The following guidelines and policy documents aim to ensure appropriate, prompt and prudent use of antimicrobials within NHSGGC:

- **Infection management guidelines (for empirical antibiotic treatment)**
- **Intravenous to Oral Switch Therapy (IVOST) Guideline**
- **Gentamicin and Vancomycin dosing guidelines**
- **Alert Antimicrobial Policy:**
  - A list of broad-spectrum agents whose use is limited to specific indications and/or on the advice of a clinical microbiologist or infectious diseases physician.
- **Antibiotic prophylaxis in surgery**

These guidelines are reviewed and updated at regular intervals. The most up to date information can be found on StaffNet, Clinical Guideline Electronic Resource Directory, and search in 'Infections' section.

## Steps to Prudent Antimicrobial Prescribing

Antibiotics are overused, particularly in elderly patients, those with urinary catheters/bacteria in their urine but no signs or symptoms of urinary tract infection and patients with viral or non-infective exacerbations of COPD.

To ensure appropriate and prudent antimicrobial prescribing follow the steps below:

- Establish a clinical diagnosis to minimise unnecessary exposure to antimicrobials.
- Prescribe when clinically justified: there is a clear site of infection, sepsis syndrome is present (see page 211 for sepsis criteria) or there is clinical deterioration.
- Patient and drug specific factors may affect antibiotic choice so look at:
  - Previous antimicrobial history
  - Previous infection with multiresistant organisms (check previous culture results)
  - Allergy (list of penicillins on page 204)
  - Renal / hepatic function
  - Other medication (see Appendix 1 of the BNF for information on drug interactions)
  - Availability and absorption by the oral route.
- Document the antibiotic indication, signs and symptoms of infection and duration of antibiotic therapy or review date in the patient's notes. Document the duration / review date on the kardex after the first dose has been given.
- Prescribe IV only for those with severe / deep seated infections, sepsis syndrome (see page 211) or if the oral route is unavailable. Review IV antibiotics daily and switch to oral when appropriate (see IVOST page 205).

- In patients with sepsis –
  - Start IV antibiotic therapy (including gentamicin) as soon as possible and within 1 hour after recognising the signs of sepsis or severe sepsis. Each hour of delay in administering IV antibiotic therapy is associated with increasing mortality (see page 211).
  - Record the first dose of antibiotic on the 'one-off' section of the kardex, so that it is administered immediately
  - Communicate with the member of staff who is responsible for administration of the IV antibiotic therapy so it is given promptly
  - Administer the antibiotic in the clinical area where infection has been recognised and do not delay until arrival at destination ward.
- Review empirical (best guess) antimicrobial therapy no later than 48 hours after initiation. Simplify and switch to narrow spectrum therapy when microbiology results become available.
- Prescribe Alert Antibiotics only for the specific indications listed (see pages 208 - 210). Document the specific indication in the patient's notes and follow the policy outlined on page 207 to obtain a supply. For indications out with those listed contact microbiology / infectious diseases unit.
- Minimise antibiotic expenditure.

## Reducing the risk of *Clostridium difficile* through prudent prescribing

*Clostridium difficile* infection (CDI) is an important healthcare associated infection in Scottish hospitals. It is life-threatening (reported mortality rate 10 - 30%) and has the potential for person to person spread within healthcare settings. Particularly at risk are patients who are aged > 65 years, frail, immunocompromised or who have chronic obstructive pulmonary disease or cardiovascular disease.

Antibiotic therapy disturbs the normal gastrointestinal flora, depleting organisms which are protective against CDI. **Any** antibiotic may be associated; those associated most commonly are listed below. Other broad spectrum agents (particularly the carbapenems) are also likely to show an association as prescribing increases. Overall antibiotic exposure, including excessive duration of therapy is also a risk factor for CDI as is surgical prophylaxis (with cephalosporins and quinolones). Proton pump inhibitors and $H_2$ antagonists also increase gastric pH which is associated with an increase in the risk of *Clostridium difficile* acquisition.

### Factors associated with CDI:

- Increasing age
- Severe underlying disease
- Non-surgical gastrointestinal procedures
- Nasogastric tube
- Long stay in hospital
- Stay in intensive care

*Continues on next page*

*Factors associated with CDI continued from previous page*

- Antibiotic use (clindamycin, cephalosporins, co-amoxiclav, ciprofloxacin (and other quinolones) and piperacillin / tazobactam)
- Longer duration of antibiotic course
- Proton pump inhibitors or $H_2$ antagonists

The antimicrobial guidelines are designed to reduce the risk of CDI by limiting overall antibiotic exposure (reduced prescriptions and duration of therapy) and by limiting those agents which have the strongest association.

# Gentamicin and Vancomycin: Reducing Patient Risk

Gentamicin and vancomycin prescribing within NHSGGC has increased in recent years. Both agents have a narrow therapeutic index i.e. efficacy or the risk of toxicity or treatment failure is related to small changes in concentration of the drugs and hence the accuracy of the dosing. In addition, gentamicin accumulates in the inner ear risking oto-vestibular toxicity if prolonged or recurrent treatment courses. Consequently, accurate prescribing, appropriate therapeutic drug monitoring (TDM) and, in the case of gentamicin, restricted duration of therapy and avoidance of repeat courses are important to minimise risk.

**NOTE**: Before prescribing these agents ensure you refer to the correct dosing and monitoring guidance and use the correct prescription and monitoring documentation.

- Gentamicin: used and prescribed in 3 distinct ways within NHSGGC adult antimicrobial policy
  - Treatment dose (see page 262)
  - Synergistic **low dose** for endocarditis (see page 216)
  - Surgical prophylaxis dose (see page 259 and StaffNet)
- Vancomycin: used and prescribed in 3 distinct ways within NHSGGC adult antimicrobial policy
  - Pulsed IV Infusion (see page 266)
  - Continuous IV Infusion (see page 270)
  - Oral Vancomycin for the local treatment of *C. difficile.* Oral Vancomycin is not absorbed and cannot be used to treat a systemic infection.

# Antibiotic Allergy and Interactions

## Allergy

- Specifically enquire as to the nature of "allergy". Abdominal pain, nausea, vomiting or dyspepsia does not constitute allergy.
- Document both the allergy and the nature of the allergy in the patient's medical notes and on the drug kardex.
- Do not give penicillin, cephalosporin or other beta-lactam* antibiotic if patient has a history of anaphylaxis, urticaria, or rash immediately after penicillin administration.
- Adults with a history of a minor rash (e.g. non-confluent, non-pruritic rash restricted to a small area of the body), or a rash that occurs > 3 days after starting an antibiotic course are unlikely to have an antibiotic allergy and therefore the antibiotic should not be withheld unnecessarily for serious infections.
- Penicillin allergy occurs in 1-10% of patients. Anaphylaxis occurs in < 0.05% of treated patients.
- Co-trimoxazole: rash occurs in ≥ 1 in 100 patients prescribed co-trimoxazole. If a rash occurs discontinue co-trimoxazole immediately.
- Be aware of the components of antibiotic co-formulations e.g. co-trimoxazole (trimethoprim and sulphamethoxazole), co-amoxiclav (amoxicillin and clavulanic acid).
- For further advice on antibiotic allergy please contact the allergy service – see Appendix 6 for contact detail.

***Beta-lactam antibiotics include**: amoxicillin; ampicillin; benzylpenicillin (Penicillin G); co-amoxiclav (Augmentin®); flucloxacillin; phenoxymethylpenicillin (Penicillin V); piperacillin / tazobactam (Tazocin®), cefaclor; cefalexin; cefotaxime; ceftazidime; ceftriaxone; cefuroxime; aztreonam; meropenem; imipenem with cilastatin, doripenem, ertapenem (see BNF for more details).

## Important Antibiotic Drug Interactions

This is not a comprehensive list; for further information refer to a pharmacist or Appendix 1 of the BNF.

**Clarithromycin**: numerous interactions (some potentially life-threatening) via;

i) Enzyme inhibition e.g. carbamazepine and simvastatin (see BNF Appendix 1).

ii) QT prolongation e.g. citalopram, fluconazole; seek advice from pharmacy. Consider other medical risk factors for QT prolongation. Also see page 7 (Assessing Medicines on Admission in Acute Patients) and Postscript Extra article on drug induced QT prolongation at www.ggcprescribing.scot.nhs.uk.

**Rifampicin**: numerous interactions through enzyme induction (see BNF Appendix 1).

**Statins**: Avoid concomitant use with macrolides and sodium fusidate (consult BNF for details). Consider using an alternative antibiotic class; liaise with microbiology / infectious diseases unit where appropriate.

**Warfarin**: INR may be altered by many antibiotics, particularly if a course is prolonged (check BNF Appendix 1).

**Oral contraceptive pill**: no additional contraceptive precautions are now required when combined oral contraceptives are used with antibiotics which do not induce liver enzymes, unless diarrhoea or vomiting occur (see BNF for advice).

# IV-Oral Antibiotic Switch Therapy (IVOST) Guideline

Intravenous therapy is appropriate in patients with:

- Sepsis: see page 211
- Clinical symptoms / signs of infection and deteriorating clinical condition
- Febrile with neutropenia / immunosuppression
- Meningitis / CNS infection
- Infective endocarditis
- Bronchiectasis
- Bone / joint infection
- Deep abscess
- Cystic fibrosis
- *Staphylococcus aureus* bacteraemia
- Skin and Soft Tissue infection, IV therapy if sepsis or 2 or more of heat, erythema or induration / swelling (IV therapy usually 2-4 days).
- Oral route compromised – vomiting, nil-by-mouth, reduced gastrointestinal absorption, mechanical swallowing disorder, unconscious.
- No oral formulation of the antibiotic available.
- Initial therapy for Biliary Sepsis / Intra-abdominal infection

**Note**: CRP does not reflect the severity of infection and may remain elevated even when infection is resolving. It cannot be used in isolation to assess the severity of infection and hence the need for IV therapy.

If none of the above apply, check microbiology results and switch to an oral narrow spectrum agent whenever possible. If no microbiology results are available use the table on the next page to guide the switch to oral therapy.

*Continues on next page*

**Table 1 – Antibiotic IV to oral switch**

| IV antibiotic | Oral antibiotic |
|---|---|
| Amoxicillin | Amoxicillin 500 mg - 1 g 8 hourly |
| Amoxicillin + Gentamicin<br>(for pyelonephritis with sepsis) | Co-amoxiclav 625 mg 8 hourly (assuming narrow spectrum agent not appropriate). |
| Benzylpenicillin | Amoxicillin 500 mg - 1 g 8 hourly (for suspected pneumococcal infection).<br>Phenoxymethylpenicillin ( Pen V) 500 mg 6 hourly or 1 g 12 hourly (for pharyngitis / tonsillitis). |
| Clarithromycin | Clarithromycin 500 mg 12 hourly |
| Clindamycin | Clindamycin is indicated in: suspected necrotising fasciitis, severe / rapidly progressive skin and soft tissue infection, possible streptococcal / staphylococcal toxic shock or severe pharyngitis.<br>Clindamycin 450 mg 8 hourly (< 70 kg)<br>Clindamycin 600 mg 8 hourly (≥ 70 kg) |
| Co-amoxiclav | Is there a narrow spectrum alternative? (e.g. Amoxicillin 500 mg - 1 g 8 hourly) otherwise Co-amoxiclav 625 mg 8 hourly |
| Co-trimoxazole | Co-trimoxazole 960 mg 12 hourly (unless PCP or multi-resistant infections in which case seek advice from microbiology / infectious diseases unit). Use trimethoprim if a sensitive organism is isolated. |
| Flucloxacillin | Flucloxacillin 500 mg -1 g 6 hourly |
| Gentamicin | Stop after a maximum of 3 - 4 days unless there is a clear clinical and microbiological need. If required for longer, seek microbiology / infectious diseases unit advice. Monitor for signs of oto and vestibular toxicity (see page 265). Consider:<br>• Is gram negative cover still required? If not stop<br>• Is there any positive microbiology? If so simplify<br>• See above / below for intra-abdominal / urinary sepsis switches. |
| Gentamicin + Amoxicillin + Metronidazole (intra-abdominal sepsis) | Co-amoxiclav 625 mg 8 hourly |
| Metronidazole | Metronidazole 400 mg 8 hourly |
| Vancomycin | Contact microbiology / infectious diseases unit for advice |
| Vancomycin + Gentamicin + Metronidazole (intra-abdominal sepsis) | Ciprofloxacin 500 mg 12 hourly + Metronidazole 400 mg 8 hourly |

Most infections will require ≤ 7 days **total** antibiotic therapy (IV and oral).

# Alert Antibiotic Policy

(The full version of the Alert Antibiotic Policy and the Alert Antibiotic Form are available on StaffNet.)

- The policy has been developed to limit the use of specific, valuable antibiotics which should be reserved for special circumstances (e.g. resistant organisms). These agents are rarely justifiable in community acquired infection.
- The agents are identified by virtue of their broad spectrum of activity, potential toxicity and/or expense. In most hospital infections, first-line antibiotic therapy is appropriate, with "Alert Antibiotics" reserved for complex infections caused by organisms that are resistant to first-line antibiotic therapy.
- Table 1 on the following pages lists the alert antibiotics and their permitted indications. These antibiotics will only be issued from pharmacy on receipt of a completed Alert Antibiotic form.

## Process for authorising an "alert agent"

- During weekday working hours (0900 – 1700 hours):
  - To obtain a supply, the "Alert Antibiotics Form" must be completed and sent to pharmacy with the indent.
  - The form should be completed by prescribers, stating the indication (see next page for list). Clinical pharmacists can complete the form in conjunction with prescribers.
  - If an alert agent is being prescribed out with the permitted indications, the choice must be discussed with a microbiologist or infectious diseases physician. The reason for use and the name of the microbiologist or infectious disease physician must be recorded on the form and medical notes.
- Out-of-hours (including weekends and public holidays):
  - The prescriber should complete the "Alert Antibiotic form". Do not delay treatment if unable to complete the form; obtain an emergency supply and complete the form as soon as possible.
  - A 24 – 72 hour emergency supply can be obtained

*Continues on next page*

**Table 1 – Alert Antibiotics**

| Alert Antibiotic | Permitted Indications |
|---|---|
| **Amikacin IV** | 1. Gentamicin resistant Gram-negative infections.<br>2. In combination therapy for mycobacterial infection when oral therapy is not possible or drug resistance is suspected.<br>3. Severe neutropenic sepsis in accordance with haematology or oncology unit's sepsis protocol. |
| **Ceftaroline IV** | Only on the advice of a microbiologist or infectious diseases physician. |
| **Ceftazidime IV** | 1. Febrile neutropenia, in accordance with haematology or oncology unit's sepsis protocol.<br>2. Empiric therapy for CAPD associated peritonitis.<br>3. Exacerbation of bronchiectasis / cystic fibrosis if evidence of colonisation with *Pseudomonas* or resistant Gram-negative organism. |
| **Ceftriaxone IV** | 1. Bacterial meningitis<br>2. Enteric fever (typhoid or paratyphoid)<br>3. Brain abscess<br>4. Acute severe pelvic inflammatory disease.<br>5. Outpatient parenteral antibiotic therapy as per agreement with infection specialist. |
| **Ciprofloxacin IV** | 1. If oral route is compromised and ciprofloxacin prescribed in line with the Infection Management Guideline.<br>2. Treatment of spontaneous bacterial peritonitis for 2 days only then oral for 5 days (in line with Infection Management Guidelines, page 238).<br>3. Neutropenic patient with fever and true penicillin allergy (in line with Infection Management Guidelines, page 214). |
| **Clindamycin IV** | 1. Suspected necrotising fasciitis or severe or rapidly progressive soft tissue infection<br>2. Suspected severe streptococcal or staphylococcal sepsis / toxic shock syndrome<br>3. Second-line therapy for PCP e.g. in HIV infection<br>4. Severe pharyngitis<br>5. Surgical prophylaxis for caesarian section in a patient with true penicillin allergy |
| **Colistin IV** | Only on the advice of a microbiologist or infectious diseases physician. |

Table continues on next page

| Table 1 – Alert Antibiotics continued form previous page | |
|---|---|
| **Alert Antibiotic** | **Permitted Indications** |
| **Daptomycin IV** | Only on the advice of a microbiologist or infectious diseases physician (**N.B.** not for pneumonia) for:<br>1. Vancomycin-resistant enterococci (VRE), vancomycin-intermediate *Staphylococcus Aureus* (VISA), vancomycin-resistant *Staphylococcus aureus* (VRSA)<br>2. Non-response or allergy / intolerance to glycopeptides (not including those who develop 'red man syndrome' because vancomycin has been infused too quickly).<br>3. Outpatient parenteral antibiotic therapy as per agreement with infection specialist. |
| **Doripenem IV/ Imipenem IV** | Only on the advice of a microbiologist or infectious diseases physician. |
| **Ertapenem IV** | 1. Proven extended spectrum beta-lactamase (ESBL) infections requiring IV therapy<br>2. Outpatient parenteral antibiotic therapy as per agreement with infection specialist. |
| **Fidaxomicin** | 1. Proven *C. difficile* relapse only on the advice of an infection specialist. |
| **Levofloxacin (IV or Oral)** | 1. Suspected *Legionella* pneumonia<br>2. Second-line for suspected atypical pneumonia |
| **Linezolid (IV or Oral)** | Only on the advice of a microbiologist or infectious diseases physician for:<br>1. VRE, VISA, VRSA<br>2. Non-response or allergy / intolerance to glycopeptides (not including those who develop 'red man syndrome' because vancomycin has been infused too quickly) |
| **Meropenem** | 1. Exacerbation of bronchiectasis / cystic fibrosis if evidence of colonisation with *Pseudomonas* / resistant Gram-negative organism.<br>2. Febrile neutropenia as second-line therapy in accordance with haematology or oncology unit's sepsis protocol.<br>3. Infections due to multi-resistant (including ertapenem-resistant) organisms<br>4. Severe sepsis unresponsive to piperacillin / tazobactam and gentamicin on the advice of a microbiologist / infectious diseases physician.<br>5. In stem cell transplant / solid organ transplant or patients receiving chemotherapy for acute leukaemia who are neutropenic or on high dose steroids (> 1 mg/kg prednisolone) for Graft Versus Host Disease or rejection and having ongoing shock that is unresponsive (within 1 hour) to appropriate fluid resuscitation measures.<br>6. Brain abscess as directed by infection specialist |

Table continues on next page

| Table 1 – Alert Antibiotics continued form previous page | |
|---|---|
| **Alert Antibiotic** | **Permitted Indications** |
| **Moxifloxacin (IV or Oral)** | Drug resistant mycobacterial infections.<br>**N.B**. Due to toxicity risks (hepatotoxicity and QT interval prolongation) only on the advice of a microbiologist / infectious diseases physician |
| **Piperacillin and tazobactam** | 1. Febrile neutropenia in line with Infection Management Guidelines (page 214)<br>2. Second-line therapy for intra-abdominal sepsis not responding to amoxicillin + gentamicin + metronidazole or first-line post-operative intra-abdominal sepsis (laparotomy).<br>3. Second-line therapy for severe hospital acquired pneumonia.<br>4. Exacerbation of bronchiectasis / cystic fibrosis if evidence of colonisation with *Pseudomonas* / resistant Gram-negative organisms.<br>5. Sepsis in decompensated liver disease with associated ascites.<br>6. Subsequent episodes of intra-abdominal sepsis. |
| **Temocillin** | Proven resistant Gram-negative infections including ESBL producers on advice of an infection specialist |
| **Tigecycline** | Only on the advice of a microbiologist or infectious diseases physician. |

| **Alert Antifungals** | **Permitted Indications** |
|---|---|
| **Anidulafungin / caspofungin / micafungin / voriconazole / posaconazole / liposomal amphotericin / Abelcet** | 1. In accordance with haematology or oncology antifungal protocol.<br>2. In the treatment of invasive candidiasis protocol (see StaffNet, Clinical Guideline Electronic Resource Directory, search in 'Infections' section).<br>3. On the advice of a microbiologist or infectious diseases physician. |

# Severe systemic infections

## Definition of Sepsis

- Sepsis: clinical symptoms of infection (fever, sweats, chills or rigors, malaise, etc.) or proven infection and **at least two** of the following:
  - Temperature < 36$^{O}$C or > 38$^{O}$C; tachycardia HR > 90 bpm; tachypnoea RR > 20 breaths/minute; WCC < 4 or >12 x $10^{9}$ /L.
- Serious or severe sepsis: sepsis with any of the following:
  - SIRS 3 - 4
  - Organ dysfunction / hypoperfusion (lactic acidosis, oliguria, or confusion)
  - Hypotension (systolic BP < 90 mmHg or a reduction of 40 mmHg from baseline)

**N.B.** Signs of sepsis may be masked in: immunosuppression, the elderly and in the presence of anti-inflammatory drugs or beta-blockers. CRP does not reflect the severity of infection and may remain elevated even when infection is resolving; it cannot be used in isolation to assess the severity of infection and hence the need for IV therapy.

Mortality from sepsis and severe sepsis increases with each hour of delay in initiating IV antibiotic therapy. In patients with sepsis, aim to complete the "**Sepsis 6**" within 1 hour:

1. Oxygen therapy (target saturation 94 - 98% or 88 - 92% for those with chronic obstructive pulmonary disease).
2. IV fluids (at least 500 ml sodium chloride 0.9% in first hour)
3. Blood cultures
4. Commence IV antibiotics according to guidelines
5. Measure lactate
6. Assess urine output (consider catheterisation in some patients)

Record first dose of antibiotic in the 'one-off' section of the kardex and communicate with the member of staff who is responsible for administration of IV antibiotic therapy to ensure it is administered immediately. *Administer the antibiotic in the clinical area where infection has been recognised and do not delay until arrival at the destination ward.*

*Management of Sepsis Source Unknown continues on next page*

## Sepsis Source Unknown (not immunocompromised or neutropenic patients)

| Indication | Antibiotic therapy | Notes / Comments |
|---|---|---|
| Community acquired or Healthcare associated sepsis or severe sepsis where the source is unknown | Benzylpenicillin IV 1.2 - 2.4 g 6 hourly<br>**and**<br>Flucloxacillin IV 2 g 4 - 6 hourly<br>**and**<br>Gentamicin* IV (dosing info page 262 )<br><br>*If true penicillin / beta-lactam allergy or MRSA suspected*:<br>Vancomycin IV (dosing info page 266)<br>**and**<br>Gentamicin* IV (dosing info page 262) | *E. coli, S. aureus* and *pneumococcus* are commonest community blood culture isolates.<br>Consider meningococcal infection and *S. pyogenes* (e.g. pharyngitis, erythroderma or hypotension).<br>Consider infective endocarditis in IVDU; line-related sepsis; recent dental extraction (see page 216).<br>Consider MRSA infection – sepsis arising > 48 hours post admission, recent hospital discharge, post operative wound or line-related sepsis or sepsis in previous or current MRSA carrier<br>*Do not continue Gentamicin beyond 3 - 4 days unless on the advice of an infection specialist. If you are unsure whether > 4 days is needed, contact an infection specialist. |
| Suspected severe streptococcal infection (e.g. toxic shock, rapidly progressive soft tissue infection) | *As for Community acquired sepsis or severe sepsis where the source is unknown* **and add in:**<br>Clindamycin* IV 600 mg 6 hourly (up to 1200 mg 6 hourly) | *Alert Antibiotic - complete Alert Form<br>Seek advice from microbiology / infectious diseases unit (Appendix 6 for contact details). |
| | | Table continues on next page |

| Sepsis Source Unknown (not immunocompromised or neutropenic) continued from previous page | | |
|---|---|---|
| **Indication** | **Antibiotic therapy** | **Notes / Comments** |
| Proven *S. aureus* bacteraemia | Flucloxacillin IV 2 g 4 - 6 hourly<br>*If true beta-lactam allergy or MRSA suspected then*:<br>Vancomycin IV (dosing info on page 266)<br>Duration 14 days IV or as advised by infection specialist | Replace intravascular device if source of infection.<br>All patients require echo and investigation for possible underlying source.<br>Discuss management (including duration of therapy) with microbiology / infectious diseases unit.<br>Repeat blood cultures after 3 - 4 days of effective therapy. |
| Sepsis syndrome secondary to suspected urinary source (includes pyelonephritis with sepsis) | See pages 220 (non-pregnant women), 221 (pregnant women) and 224 (in men) | |

# Immunocompromised patients with fever

Immunocompromised patient can include the following:

- Received chemotherapy within the previous 3 weeks
- On high dose steroids e.g. prednisolone > 15 mg/day for > 2 weeks*
- On other immunosuppressive agent e.g. anti-TNF, cyclophosphamide
- Transplant patient (solid organ or bone marrow)

## Neutropenic Sepsis Definition*:

Neutrophils either < 0.5 or < 1 X $10^9$/L and falling, **and**

Temperature > 38°C or hypothermic (< 36°C) on 2 occasions, at least 30 minutes apart.

If stem cell transplant recipient, refer to Beatson Oncology protocol poster (see StaffNet)

*Patients on high dose steroids or severely immunocompromised may not have an increased temperature, but present with symptoms which may include sweats, chills, rigors, malaise, respiratory rate > 20 breaths/minute, tachycardia (> 90 bpm) or hypotension. Note that patients may appear well perfused despite hypotension.

Ensure prompt IV antibiotic administration in sepsis – see note on page 211.

| Immunocompromised patient with fever | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Neutropenia | Piperacillin / Tazobactam* IV 4.5 g 6 hourly<br>**and**<br>Gentamicin** IV (dosing info page 262)<br>*If suspected staphylococcal infection (e.g. line-related sepsis or soft tissue infection)* **to the above add in**:<br>Vancomycin IV (dosing info page 266)<br>*If true penicillin / beta-lactam allergy*:<br>Vancomycin IV (dosing info page 266)<br>**and**<br>Gentamicin** IV (dosing info page 262)<br>**and**<br>Ciprofloxacin* IV 400 mg 12 hourly | Investigate for source of sepsis.<br>Review treatment daily.<br>*Piperacillin / Tazobactam or Ciprofloxacin:<br>• Reduce dose in renal impairment (see BNF).<br>• Alert antibiotic, please complete Alert Form.<br>• QTc prolongation<br>**Gentamicin:<br>• Do not prescribe in myeloma patients unless discussed with relevant haematologist.<br>Discuss treatment with appropriate specialist and seek microbiology / infectious diseases unit for advice (Appendix 6 for contact details). |

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| Table continued form previous page | | |
|---|---|---|
| **Immunocompromised patient with fever** | **Antibiotic Therapy** | **Notes / Comments** |
| In stem cell transplant / solid organ transplant or patients receiving chemotherapy for acute leukaemia<br>**and**<br>neutropenic or on high dose steroids (> 1 mg/kg prednisolone) for Graft Versus Host Disease or rejection<br>**and**<br>shocked** | Meropenem* IV 1 g 8 hourly<br>**and**<br>Amikacin* IV (dosing info page 261) | Consider multi-resistant organisms.<br>* Alert antibiotic – please complete form.<br>** Shocked = requiring inotropic support or systolic BP < 90 mmHg, unresponsive (within 1 hour) to appropriate fluid resuscitation measures. |
| Immunocompromised (excluding stem cell transplant patients) with fever **and no neutropenia** | Manage as per infection management guidelines based on anatomical source. | Consider additional serious fungal or viral infection. Discuss with appropriate specialist and seek microbiology / infectious diseases unit for advice (Appendix 6 for contact details) |
| HIV positive patient with fever | Manage as per infection management guidelines based on anatomical source. | Contact infectious diseases consultant on call (Appendix 6 for contact details) |

# Endocarditis

- Take three sets of blood cultures. For each set send blood culture in aerobic and anaerobic bottles.
- Seek senior specialist advice, refer to cardiology and consider early cardiothoracic input, particularly in Staphylococcal infections and infections involving a prosthetic valve.
- Use **synergistic dosing** of gentamicin:
  - IV 80 mg 12 hourly, administer as a bolus over 3 - 5 minutes.
  - Measure concentration 1 hour after dose administration and immediately before the next dose.

Seek dosing and monitoring advice from pharmacy within 24 hours of starting.

  - Duration is dependent on the organism; seek advice from microbiology / infectious diseases unit.
  - Monitor renal function daily and gentamicin concentrations at least every 2 - 3 days.
  - Monitor for oto / vestibular toxicity (see page 265).
- Discuss all suspected endocarditis cases with microbiology or infectious diseases unit and with cardiology.
- Consider OPAT referral after at least first week of inpatient therapy.

| Endocarditis Empirical therapy | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Native heart valves<br>*(Streptococcus viridans, Staphylococcus aureus,* enterococcal species)<br>*Streptococcus pyogenes* may also be implicated in IVDU | Amoxicillin IV 2 g 4 hourly<br>**and**<br>Flucloxacillin IV 2 g 4 hourly<br>**and**<br>Gentamicin* IV (synergistic dosing)<br><br>*If true penicillin / beta-lactam allergy / penicillin resistance / suspected MRSA infection:*<br>Vancomycin IV (dosing info page 266)<br>**and**<br>Gentamicin* IV (synergistic dosing) | Discuss ongoing therapy in all cases with microbiology / infectious diseases unit.<br>Acute or rapidly progressive infection is suggestive of *S. aureus* infection<br>Gentamicin* synergistic dosing – contact pharmacists for dosing advice.<br>Monitor gentamicin concentrations at least every 2 - 3 days. Aim for peak concentration (1 hour post-dose) of 3 – 5 mg/L and a trough (pre-dose) of < 1 mg/L.<br>Gentamicin course durations as per microbiology / infectious diseases unit / cardiology advice. Usually:<br>• *Staphylococcus aureus* infection: 3 - 5 days<br>• Enterococcal infection: 4 - 6 weeks<br>• Penicillin sensitive Streptococcal infections – gentamicin not required. |

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| Endocarditis Empirical therapy | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Prosthetic heart valve<br>Infections are usually:<br>• Staphylococcal (Coagulase negative / MSSA / MRSA)<br>• Enterococcal | Vancomycin IV (dosing info page 266)<br>**and**<br>Gentamicin* IV (synergistic dosing) for first 2 weeks<br>**and**<br>Rifampicin** oral<br>≤ 70 kg 450 mg 12 hourly<br>> 70 kg 600 mg 12 hourly<br>*Or in place of rifampicin add*: Sodium Fusidate** oral 500 mg 8 hourly (or if suspension then fusidic acid** oral 750 mg 8 hourly) | Discuss all cases with microbiology / infectious diseases unit.<br>If Meticillin Sensitive *Staphylococcus aureus* (MSSA) isolated, switch from vancomycin to flucloxacillin.<br>*Gentamicin synergistic dosing - contact pharmacists for dosing advice.<br>Gentamicin concentrations - aim for peak concentration (1 hour post-dose) of 3 – 5 mg/L and a trough (pre-dose) of < 1 mg/L.<br>**Rifampcin / Sodium Fusidate (fusidic acid)<br>• Check for drug interactions (BNF Appendix 1)<br>• Caution if pre-existing liver disease<br>• Must not be used as monotherapy |

## Further management

Discuss further management with microbiology or infectious diseases unit.

# Urinary tract infections (UTIs)

- Antibiotics are overused in the elderly particularly in patients with urinary catheters or suspected UTIs. Consider delaying antibiotic therapy pending culture.
- Do not treat asymptomatic bacteriuria, except in pregnancy.
- If antibiotic therapy appropriate, only prescribe after urine cultures have been taken, unless sepsis when blood cultures should be taken and antibiotic therapy not delayed.

*Continues on next page*

| UTI in non-pregnant women | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Uncomplicated lower UTI i.e. no fever or flank pain<br>(*Coliforms (especially E. coli), as well as Enterococci and Staphylococcus saprophyticus*) | Prescribe only if urinary symptoms:<br>Trimethoprim* oral 200 mg 12 hourly<br>**or**<br>Nitrofurantoin oral 50 mg 6 hourly (avoid if G6PD deficiency or eGFR < 60 ml/minute/1.73m$^2$)<br>Total course duration: 3 days. | Urinary symptoms:<br>Cystitis, dysuria, frequency.<br>*eGFR < 30 ml/minute/1.73m$^2$: Co-amoxiclav oral 625 mg 12 hourly.<br>If eGFR < 10 ml/minute/1.73m$^2$: Contact renal pharmacist (see Appendix 6 for contact details)<br>*If true penicillin / beta lactam allergy* **and** eGFR < 30 ml/minute/1.73m$^2$ : Ciprofloxacin 250 mg oral 12 hourly for 7 days. **Note:** Ciprofloxacin QTc prolongation. |
| Upper UTI ***without sepsis*** | Trimethoprim* oral 200 mg 12 hourly for 14 days<br>or if resistant organism** suspected :<br>Co-amoxiclav oral 625 mg 8 hourly for 14 days<br>or<br>Ciprofloxacin# oral 500 mg 12 hourly for 7 days | Symptoms: Loin pain, flank tenderness, dysuria.<br>For manifestations of sepsis (see page 211).<br>**Sensitive organism suspected - sensitive organism suggested by no previous resistant isolates, no history of recurrent UTIs, no history of antibiotic exposure in prior 3 months and no pre – existing renal tract abnormality (including stones) or device (e.g. stent).<br>*eGFR < 30 ml/minute/1.73m$^2$: Co-amoxiclav oral 625 mg 12 hourly.<br>*eGFR < 10 ml/minute/1.73m$^2$: Contact renal pharmacist (see Appendix 6 for contact details)<br># eGFR < 30 ml/minute/1.73m$^2$: Ciprofloxacin 250 mg oral 12 hourly for 7 days. **Note**: Ciprofloxacin QTc prolongation. |

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| UTI in non-pregnant women | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Upper UTI **with sepsis** (includes pyelonephritis with sepsis)<br>(Coliforms, *P. aeruginosa* in chronic disease) | Amoxicillin IV 1 g 8 hourly<br>**and**<br>Gentamicin* IV (dosing info page 262) for 2 doses then simplify according to sensitivities<br>**or** *if true penicillin / beta-lactam allergy:*<br>Gentamicin* IV monotherapy (dosing info page 262)<br>Total course duration (IV and oral) 14 days | IV antibiotic administration in sepsis – see note on page 211.<br>Adjust antibiotic therapy when culture results are available<br>*Do not use gentamicin beyond 3 - 4 days. Discuss alternatives with microbiology / infectious diseases unit.<br>Amoxicillin PLUS gentamicin is the preferred regime for urosepsis.<br>Where IV therapy is required and a trimethoprim-sensitive organism has been isolated IV co-trimoxazole 960 mg 12 hourly may be used unless eGFR < 30 ml/minute/1.73m$^2$. |
| **UTI in pregnant women** | **Antibiotic Therapy** | **Notes / Comments** |
| Asymptomatic bacteriuria | Treat according to culture results.<br>Total course duration: 3 - 7 days. | • Culture prior to treatment.<br>• Treat asymptomatic bacteruria in pregnancy.<br>• Re-culture 7 days after completion of course.<br>• Refer to BNF for information on the use of antibiotics in pregnancy.<br>Trimethoprim in 1st trimester– ensure folic acid supplement is given.<br>Trimethoprim (theoretical risk in first trimester in patients with poor diet as folate antagonist). Further information is available on www.toxbase.org<br>*eGFR < 30ml/minute/1.73m$^2$: Co-amoxiclav oral 625 mg 12 hourly.<br>eGFR < 10 ml/minute/1.73m$^2$: Contact renal pharmacist (see Appendix 6 for contact details). *If true penicillin / beta-lactam allergy*, discuss with microbiology |
| Lower UTI ***without sepsis*** | 1st / 2nd trimester –<br>Nitrofurantoin oral 50 mg 6 hourly (avoid if G6PD deficiency or eGFR < 60 ml/minute/1.73m$^2$; contact microbiology for an alternative)<br>3rd trimester –<br>Trimethoprim* oral 200 mg 12 hourly<br>Total course duration: 7 days | |
| | Table continues on next page | |

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| UTI in pregnant women | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Upper UTI ***without sepsis*** | Co-amoxiclav oral 625 mg 8 hourly<br>*If true penicillin / beta-lactam allergy:*<br>Trimethoprim* oral 200 mg 12 hourly<br>Total course duration: 14 days | *eGFR < 30ml/minute/1.73m$^2$: Co-amoxiclav oral 625 mg 12 hourly.<br>*eGFR < 10 ml/minute/1.73m$^2$: Contact renal pharmacist (see Appendix 6 for contact details).<br>*If true penicillin / beta-lactam allergy,* discuss with microbiology. |
| Upper UTI / pyelonephritis ***with sepsis*** | Co-amoxiclav IV 1.2 g 8 hourly<br>Total course duration 14 days (IV and oral)<br>*If true penicillin / beta-lactam allergy*:<br>Gentamicin* IV (dosing info page 262).<br>Contact microbiology for oral or alternative IV options.<br>Do not continue gentamicin beyond 4 days. | IV antibiotic administration in sepsis – see note on page 211.<br>Co-amoxiclav – IV to oral switch see page 205.<br>Culture prior to treatment.<br>Re-culture 7 days after completion of course.<br>*Gentamicin - If pre-pregnant BMI > 30 then 5 mg/kg of non-pregnant weight. Maximum gentamicin dose of 600 mg. Measure concentration 1 hour post dose and a second sample 6 - 14 hours post dose and seek advice from pharmacy. |
| Table continues on next page – Therapy for MEN | | |

Table continued from previous page

| UTI in men | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Cystitis / lower UTI in men *i.e. without sepsis or suspected prostatitis or epididymitis* | Trimethoprim* oral 200 mg 12 hourly<br>**or**<br>Nitrofurantoin oral 50 mg 6 hourly (avoid if G6PD deficiency or eGFR < 60 ml/minute/1.73m$^2$)<br>Total course duration 7 days. | Symptoms: dysuria, urgency, frequency, polyuria, suprapubic tenderness.<br>*eGFR < 30 ml/minute/1.73m$^2$: Co-amoxiclav oral 625 mg 12 hourly.<br>If eGFR < 10 ml/minute/1.73m$^2$: Contact renal pharmacist (see Appendix 6 for contact details).<br>*If true penicillin / beta-lactam allergy and eGFR < 30 ml/minute/1.73m$^2$:* Ciprofloxacin 250 mg oral 12 hourly. **Note**: Ciprofloxacin QTc prolongation |
| Acute prostatitis<br>(*E. coli, Klebsiella, Proteus*) | Trimethoprim* oral 200 mg 12 hourly<br>**or** if resistant organism or failure to improve with above:<br>Ciprofloxacin# oral 500 mg 12 hourly<br>Total course duration 14 days and review response.** | Refer to Urology. Modify antibiotic therapy depending on urinary culture results and clinical response.<br>*If eGFR < 30 ml minute/1.73m$^2$:<br>Co-amoxiclav oral 625 mg 12 hourly.<br>*eGFR < 10 ml/minute/1.73m$^2$: Contact renal pharmacist (see Appendix 6 for contact details).<br>*If eGFR < 30 ml minute/1.73m$^2$ **and** *true penicillin / beta-lactam allergy:*<br>#Ciprofloxacin 250 mg oral 12 hourly (**Note**: QTc prolongation)<br>**Longer courses of 4 - 6 weeks may be required if continued symptoms or if culture positive. |

Table continues on next page – Therapy for MEN

Table continued from previous page – Therapy for MEN

| UTI in men | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Epididymitis / orchitis | Ofloxacin# oral<br>200 mg 12 hourly for 14 days.<br>If risk of *N.gonorrhoeae* / *C. trachomatis*:<br>Refer to GUM (see Appendix 6 under Sandyford for contact details). | #Ofloxacin: QTc prolongation<br>Exclude testicular torsion.<br>Consider mumps in young adults when associated with parotitis (antibiotics not required).<br>Perform MSSU and send a further 1st void urine sample to virology (white top universal) for Nucleic Acid Amplification Tests (NAAT) for Chlamydia and Gonococcus. Urethral swab if discharge.<br>If age < 35 years, sexually active or urethral discharge, refer to GUM. |
| Upper UTI ***without sepsis*** | Trimethoprim* oral 200 mg 12 hourly (if a sensitive organism is suspected)** for 14 days<br>**or** if resistant organism suspected:<br>Co-amoxiclav oral 625 mg 8 hourly for 14 days<br>**or** *if true penicillin / beta-lactam allergy:*<br>Ciprofloxacin# oral 500 mg 12 hourly for 7 days. | Symptoms: loin pain, flank tenderness, dysuria<br>For manifestations of sepsis (see page 211)<br>*If eGFR < 30ml/minute/1.73m$^2$: Co-amoxiclav oral 625 mg 12 hourly.<br>*eGFR < 10 ml/minute/1.73m$^2$: Contact renal pharmacist (see Appendix 6 for contact details).<br>#If eGFR < 30 ml minute/1.73m$^2$ **and** *true penicillin / beta-lactam allergy*: #Ciprofloxacin 250 mg oral 12 hourly (**Note**: QTc prolongation).<br>**Sensitive organism suggested by no previous resistant isolates, no history of recurrent UTIs, no history of antibiotic exposure in prior 3 months and no pre – existing renal tract abnormality (including stones) or device (e.g. stent). |

Table continues on next page – Therapy for MEN

Table continued from previous page – Therapy for MEN

| UTI in men | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Upper UTI ***with sepsis***<br>(includes pyelonephritis with sepsis)<br>(Coliforms, *P. aeruginosa* in chronic disease) | Amoxicillin IV 1 g 8 hourly<br>**and**<br>Gentamicin* IV (dosing info page 262) for 2 doses then simplify according to sensitivities<br>**or** *if true penicillin / beta-lactam allergy:*<br>Gentamicin* IV monotherapy (dosing info page 262)<br>Total course duration (IV and oral) 14 days | IV antibiotic administration in sepsis – see note on page 211.<br>Adjust antibiotic therapy when culture results are available.<br>*Do not use gentamicin beyond 3 - 4 days. Discuss alternatives with microbiology / infectious diseases unit.<br>Amoxicillin PLUS gentamicin is the preferred regime for urosepsis.<br>Where IV therapy is required and a trimethoprim sensitive organism has been isolated IV co-trimoxazole 960 mg 12 hourly may be used unless eGFR < 30ml/minute/1.73m$^2$. |

| Catheter-related UTI | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Asymptomatic bacteriuria | Antibiotic therapy not recommended | |
| Symptomatic bacteriuria ***without sepsis*** | Remove / replace catheter – culture urine.<br>Give a **single** dose of gentamicin IV immediately prior to removal (dosing info page 262). | Symptoms:<br>• Fever<br>• Flank or suprapubic discomfort<br>• Nausea / vomiting<br>• New onset confusion<br>• Cloudy or offensive urine |
| Symptomatic bacteriuria ***with sepsis*** | • Remove / replace catheter – culture urine.<br>• Give a single dose of gentamicin* IV (dosing info page 262).<br>• Prescribe according to culture results. If not available prescribe as per pyelonephritis on previous pages.<br>Total course duration 7 days (IV and oral). | IV antibiotic administration in sepsis and for definition of sepsis see page 211.<br>Adjust antibiotic therapy when culture results are available.<br>*Do not use gentamicin beyond 3 - 4 days. Discuss alternatives with microbiology / infectious diseases unit.<br>Where IV therapy is required and a trimethoprim sensitive organism has been isolated IV co-trimoxazole 960mg 12 hourly may be used unless eGFR < 30 ml/minute/1.73m$^2$). |
| **Query UTI / LRTI** | **Antibiotic Therapy** | **Notes / Comments** |
| ? UTI / LRTI | Manage according to individual UTI and LRTI guidelines ( see pages 230 - 235).<br>If sepsis syndrome, treat as per sepsis of unknown origin (see pages 212). | See page 148 for diagnosis of pneumonia.<br>Do not treat asymptomatic bacteruria. |

# Upper respiratory tract infections

| Upper respiratory tract infection | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Tonsillitis / Pharyngitis<br>(Non-severe / able to swallow) | Viral (common cause) – not routinely recommended.<br>Bacterial:<br>Phenoxymethylpenicillin* oral 500 mg 6 hourly or 1 g 12 hourly for 10 days in total<br>*If true penicillin / beta-lactam allergy*:<br>Clarithromycin** oral 500 mg 12 hourly **for 5 days** | Bacterial cause commonly *Streptococcus pyogenes*.<br>*Give IV only in severe cases (see below).<br>**Clarithromycin – serious drug interactions (see BNF Appendix 1) and QTc prolongation. |
| Tonsillitis / Pharyngitis (unable to swallow)<br>If severe sepsis – see below | Benzylpenicillin IV 1.8 g 6 hourly<br>Total duration 10 days (IV and oral)<br>*If true penicillin / beta-lactam allergy*:<br>Clarithromycin* IV 500 mg 12 hourly **for 5 days** | *If severe swallowing problems or suspected quinsy refer urgently to ENT.*<br>*Clarithromycin – serious drug interactions (see BNF Appendix 1) and QTc prolongation).<br>**Alert antibiotic - complete Alert Form. |
| Tonsillitis / Pharyngitis (severe sepsis, including hypotension or erythroderma) | Benzylpenicillin IV 1.8 g 4 hourly<br>**and**<br>Clindamycin** IV 600 mg 6 hourly<br>*If true penicillin / beta-lactam allergy*:<br>Vancomycin IV (dosing info page 266)<br>**and**<br>Clindamycin** IV 600 mg 6 hourly<br>Total course duration (IV and oral) 10 days. | |

Table continues on next page

Table continued from previous page

| Upper respiratory tract infection | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Otitis media | Antibiotics not usually required.<br><br>Amoxicillin oral 500 mg - 1g 8 hourly<br><br>**or** *if true penicillin / beta-lactam allergy:*<br><br>Clarithromycin* oral 500 mg 12 hourly<br><br>Total duration 5 days. | Usually viral or self limiting – discuss with microbiology.<br><br>Poor outcome unlikely if no vomiting or temperature < 38.5°C. Use non-steroidal anti-inflammatory drugs or paracetamol. Antibiotics do not reduce pain in first 24 hours, subsequent attacks or deafness.<br><br>*Haemophilus* is an extracellular pathogen, thus macrolides, which concentrate intracellularly, are less effective treatment.<br><br>Antibiotic therapy if persistent or progressive symptoms despite symptomatic therapy.<br><br>*Clarithromycin – serious drug interactions (see BNF Appendix 1) and QTc prolongation |

Table continues on next page

Table continued from previous page

| Upper respiratory tract infection | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Otitis Externa | Only if infection / cellulitis present:<br>Local measures important*<br>Neomycin / Betamethasone drops (Betnesol N®) 2 - 3 drops 3 - 4 times daily<br>**or**<br>Neomycin / Dexamethasone spray (Otomize®) 1 puff three times a day<br>**or**<br>Gentamicin / Hydrocortisone (Gentisone HC®) 2 - 3 drops, 3 - 4 times daily and at night.<br>Total duration 7 days | Many cases recover after thorough cleansing of external ear canal, by suction or dry mopping.<br>*1. Treat inflammation and infection<br>2. Control pain<br>3. Avoid promoting factors *i.e. cotton buds, shampoo, water, swimming, leave hearing aid out if used.*<br>4. Follow up and culture recalcitrant cases.<br>Refer to local ENT early if diabetic, immunocompromised, cellulitis or disease extending outside ear canal, recent ear surgery, systemic upset, severe infection / canal stenosis with excess debris. |
| Conjunctivitis | Chloramphenicol topical 0.5% eye drops, 1 drop 2 hourly. Reduce to 6 hourly with clinical improvement<br>**and**<br>Chloramphenicol 1% eye ointment apply at night<br>Duration: 48 hours after resolution | Most bacterial infections are self-limiting (65% resolve on placebo). They are usually unilateral with yellow-white mucopurulent discharge.<br>Refer to ophthalmology if not resolving or if visual disturbance. |

Table continues on next page

Table continued from previous page

| Upper respiratory tract infection | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Acute Sinusitis | Consider:<br>Xylometazoline 0.1% nasal spray, 1 spray into each nostril up to 8 hourly (maximum duration 7 days as longer duration can cause rebound congestion).<br>If antibiotic therapy indicated*:<br>Amoxicillin oral 500 mg 8 hourly (1 g 8 hourly if severe)<br>**or**<br>Doxycycline oral 200 mg as a one-off single dose followed by 100 mg every 24 hours<br>Total duration 7 days | **Symptomatic benefit of antibiotics is small**<br>69% resolve in 7 - 10 days without antibiotics; and 80% resolve in 14 days without antibiotics.<br>*Reserve antibiotics for severe or persistent symptoms (> 10 days). |

# Lower respiratory tract infections (LRTI)

(Also see page 138 for management of acute COPD exacerbation.)

| Lower respiratory tract infections (not pneumonia) | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Infective exacerbation of COPD<br>Purulent bronchitis<br>LRTI and pre-existing lung disease | Amoxicillin oral 500 mg 8 hourly<br>**or**<br>Doxycycline oral 200 mg as one-off single dose followed by 100 mg daily<br>**or**<br>Clarithromycin* oral 500 mg 12 hourly<br>Total course duration 5 days. | IV administration in sepsis – see note on page 211.<br>Likely organisms:<br>*Pneumococcus, Haemophilus influenzae, Moraxella catarrhalis*.<br>Antibiotic:<br>• Prescribe antibiotic only if purulent sputum.<br>• Antibiotic choice depends on previous antibiotic therapy or if true penicillin / beta-lactam allergy.<br>*Clarithromycin activity vs *Haemophilus* is reduced compared to other agents<br>Clarithromycin – serious drug interactions (see BNF Appendix 1) and QTc prolongation |
| Severe / complicated exacerbation:<br>• Ventilation required or<br>• Sepsis or<br>• Other indication for IV route | Amoxicillin IV 1 g 8 hourly<br>**or**<br>Clarithromycin* IV 500 mg 12 hourly<br>Review IV therapy daily. Total course duration 7 days (IV and oral). | |

*Lower respiratory tract infections continue on next page*

# Pneumonia

(Also see page 148 for management of community acquired pneumonia – CAP)

## CURB-65 Calculation* (for community acquired pneumonia)

- New ***C***onfusion (Abbreviated Mental Test score ≤ 8 – see table below);
- ***U***rea > 7 mmol/L;
- ***Respiratory Rate*** ≥ 30 breaths/minute;
- ***B***P - systolic < 90 mmHg or, diastolic ≤ 60 mmHg;
- age ≥ 65 years

Score 1 point for each feature present.

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*Clinical judgement is essential when deciding on the management of all patients with CAP and calculating a CURB-65 score does not replace this. Each patient must be managed individually and the interpretation of the CURB-65 score is best refined through clinical judgement that takes into account all the clinical information available at the time. **For example**: a young patient with a respiratory rate of > 40 breaths/minute may warrant hospital supervised management despite a CURB-65 score of 1. Clinical judgement is especially important in patients at high risk of death (CURB-65 scores 3, 4 and 5) in whom decisions regarding intravenous administration of antibiotics or transfer to critical care facilities need to be made.

**N.B.** CURB-65 should not be used to assess the severity of conditions other than pneumonia.

### The Abbreviated Mental Test:

A score of 8 or less has been used to define mental confusion in the CURB-65 severity score.

Each question scores 1 mark - total 10 marks.

| | |
|---|---|
| 1. Age | 6. Recognition of two persons ( doctor, nurse etc) |
| 2. Date of birth | 7. Recall address (e.g. 42 West Street) |
| 3. Time (to nearest hour) | 8. Date of First World War |
| 4. Year | 9. Name of present Monarch |
| 5. Name of hospital | 10. Count backwards (20-1) |

H M Hodkinson. Evaluation of a mental test score for assessment of mental impairment in the elderly, Age Ageing (1972) 1(4): 233-238, by permission of Oxford University Press.

*Continues on next page*

**Pneumonia (continued from previous page)**

| Community Acquired Pneumonia – CAP | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| **Non-severe CAP:**<br>CURB-65 score 0 - 1 and admitted to hospital ***and no sepsis syndrome***<br>(< 3% mortality) | Amoxicillin# oral 500 mg 8 hourly<br>**or**<br>Doxycycline# oral 200 mg as one-off single dose followed by 100 mg once daily<br>**or**<br>Clarithromycin* oral 500 mg 12 hourly<br>Total course duration 7 days. | Likely organisms:<br>*Strep. pneumoniae, Haemophilus influenzae, Moraxella catarrhalis*.<br>#CAP associated with foreign travel, consider Clarithromycin first-line.<br>*Clarithromycin – serious drug interactions (see BNF Appendix 1) and QTc prolongation. |
| **Moderate CAP:**<br>CURB-65 = 2 ***and no sepsis syndrome*** (9% mortality) | Amoxicillin# oral 500 mg 8 hourly<br>**and either:**<br>Doxycycline# oral 200 mg as one-off single dose followed by 100 mg once daily<br>**or**<br>Clarithromycin* oral 500 mg 12 hourly<br>*If true penicillin / beta-lactam allergy*:<br>Clarithromycin* oral 500 mg 12 hourly (single therapy)<br>Total course duration 7 days. | Sepsis criteria – see page 211.<br>#CAP associated with foreign travel, consider Clarithromycin first-line.<br>*Clarithromycin – serious drug interactions (see BNF Appendix 1) and QTc prolongation. |
| | | Table continues on next page |

Table continued from previous page

| Community Acquired Pneumonia – CAP | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| **Severe CAP:**<br>CURB-65 score ≥ 3<br>(17 - 57% mortality)<br>**or**<br>CAP with any CURB-65 score<br>***and sepsis syndrome*** | Clarithromycin* oral or IV** 500 mg 12 hourly<br>**and either:**<br>Amoxicillin IV 1 g 8 hourly (*if not previously received any prior treatment*)<br>**or**<br>#Co-amoxiclav IV 1.2 g 8 hourly (*if previously received treatment in the community*)<br>*If true penicillin / beta-lactam allergy*:<br>Vancomycin IV (dosing info page 266)<br>**and either:**<br>Clarithromycin##* IV** 500 mg 12 hourly<br>or<br>Doxycycline## oral 200 mg as one-off single dose followed by 100 mg once daily<br>Total course duration (IV and oral) 7 - 10 days (14 days if atypical suspected or bacteraemia, 21 days if *Legionella*). | IV administration in sepsis – see note on page 211.<br>Review IV therapy daily, see IVOST policy (page 205).<br>*Clarithromycin - serious drug interactions (see BNF Appendix 1) and QTc prolongation.<br>#Consider co-amoxiclav if non-responsive to previous amoxicillin treatment.<br>##CAP associated with foreign travel, consider Clarithromycin first-line.<br>**Clarithromycin - use oral preparation if not critically unwell and high probability of pneumococcal disease unless true penicillin / beta -lactam allergy when IV route is preferred.<br>**If** critically unwell or *Legionella* suspected: Discuss with microbiology / infectious diseases consultant / respiratory physicians. |

*Continues on next page*

## Pneumonia (continued from previous page)

CURB-65 see page 231 and SIRS criteria see page 211.

| Hospital Acquired Pneumonia – HAP | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| HAP: within 4 days of hospital admission | Assess CURB-65 score / Sepsis criteria and treat as per CAP (pages 232 - 233)<br>Total course duration 7 days. | Consider alternative diagnosis e.g. sepsis syndrome, PTE<br>Organisms: Coliforms; diverse.<br>IV administration in sepsis – see note on page 211.<br>#Doxycycline - if no response at 48 hours, contact microbiology for advice.<br>*Do not continue Gentamicin beyond 3 - 4 days unless on the advice of an infection specialist. If you are unsure whether > 4 days is needed, contact an infection specialist.<br>** Ciprofloxacin QTc prolongation. IV ciprofloxacin is an Alert Antibiotic - complete alert form. |
| HAP: within 7 days of discharge from a hospital or ≥ 5 days hospital admission **and** CURB-65 score ≤ 2 ***and no sepsis*** | Co-amoxiclav oral 625 mg 8 hourly<br>**or**<br>Doxycycline# oral 200 mg as one-off single dose followed by 100 mg 12 hourly<br>Total course duration 7 days. | |
| HAP: within 7 days of discharge from a hospital or ≥ 5 days hospital admission<br>**and** CURB-65 score ≥ 3 or sepsis syndrome | Co-amoxiclav IV 1.2 g 8 hourly<br>**and**<br>Gentamicin* IV (dosing info page 262)<br>*If MRSA suspected add in*: Vancomycin IV (dosing info page 266)<br>*If true penicillin / beta-lactam allergy*: Vancomycin IV (dosing info page 266)<br>**and**<br>Ciprofloxacin** oral 500 mg 12 hourly (or Ciprofloxacin ** IV 400 mg 12 hourly if unable to swallow)<br>Total course duration (IV and oral) 7 - 10 days (14 days if atypical suspected or bacteraemia) | |

*Continues on next page*

**Pneumonia (continued from previous page)**

| Pneumonia | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Suspected *Staphylococcus aureus* pneumonia (post influenza, or chicken pox or severe bilateral / cavitatory changes) | Treat as per severe CAP (page 233) **and add in**:<br>Flucloxacillin IV 2 g 6 hourly<br>*If true penicillin / beta-lactam allergy or MRSA suspected*: Vancomycin IV (dosing info page 266)<br>**and**<br>Clarithromycin* IV 500 mg 12 hourly<br>Total course duration 10 days (IV and oral) | *Staphylococcus aureus* pneumonia is severe and life-threatening and requires admission to high dependency / ITU.<br>Discuss further management with microbiology / infectious diseases consultant and respiratory physicians.<br>*Clarithromycin – serious drug interactions (see BNF Appendix 1) and QTc prolongation. |
| Suspected aspiration pneumonia | Metronidazole IV 500 mg 8 hourly<br>**With either:**<br>Amoxicillin IV 1 g 8 hourly<br>**or**<br>Clarithromycin* IV 500 mg 12 hourly<br>Total course duration (IV and oral) 7 days. | Consider aspiration pneumonia if:<br>- history of impaired swallowing or<br>- vomiting with possible aspiration 48 hours before.<br>Infection is indicated by change in sputum quality to purulent or mucopurulent or fever and new chest x-ray changes.<br>Aspiration pneumonitis does not require antimicrobial therapy.<br>*Clarithromycin – serious drug interactions (see BNF Appendix 1) and QTc prolongation. |

# Intra-abdominal or hepatobiliary infections

| Infection | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Peritonitis or suspected intra – abdominal sepsis (≥ 2 of SIRS criteria see page 211)<br><br>(For spontaneous bacterial peritonitis see next page) | **First episode -**<br><br>Gentamicin IV (dosing info, page 262)<br>**and**<br>Amoxicillin IV 1 g 8 hourly<br>**and**<br>Metronidazole IV 500 mg 8 hourly<br><br>*If true penicillin / beta-lactam allergy*:<br>Gentamicin IV (dosing info, page 262)<br>**and**<br>Vancomycin IV (dosing info page 266)<br>**and**<br>Metronidazole IV 500 mg 8 hourly<br><br>**Subsequent episode -** discuss appropriate choice of antibiotic with microbiology.<br><br>Total course duration up to 7 days but dependent on clinical review. | Organisms associated with intra-abdominal sepsis: Coliforms, Enterococci, Streptococci e.g. *Strept milleri* and anaerobes.<br><br>Gentamicin is essential in empirical management.<br>If antibiotic therapy is required for ≥ 4 days:<br>• Refer to IVOST (page 205) if suitable for oral therapy.<br>• If IV therapy still required and no beta-lactam allergy switch to IV co-amoxiclav and consider IV to oral switch daily.<br>• If IV therapy required **and** *true beta-lactam allergy* please contact microbiology / infectious diseases unit (Appendix 6 for contact details).<br><br>**N.B**. In suspected appendicitis without sepsis (see SIRS criteria page 211) and mild diverticulitis with no evidence of perforation on CT Scan, antibiotic therapy may be withheld at the discretion of the treating surgeon. |
| Table continues on next page | | |

Table continued from previous page

| Infection | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Biliary tract infection (Cholangitis, cholecystitis) | Gentamicin# IV (dosing info page 262)<br>**and**<br>Amoxicillin IV 1 g 8 hourly<br>**and**<br>Metronidazole IV 500 mg 8 hourly<br>*In frail elderly patients or eGFR < 50ml/minute/1.73m²:*<br>Single therapy with Piperacillin / tazobactam IV 4.5 g 8 hourly*<br>*If true penicillin / beta-lactam allergy*:<br>Gentamicin IV (dosing info page 262)<br>**and**<br>Vancomycin IV (dosing info page 266)<br>**and**<br>Metronidazole IV 500 mg 8 hourly<br>Total duration: Subject to regular clinical review and no more than 7 days in total. | Anaerobes are rare in biliary tract infections but are associated with a more severe clinical illness.<br>Antibiotics are not indicated for:<br>• Biliary colic in the absence of sepsis<br>• Acute pancreatitis unless there is co-existent cholangitis, suggested by jaundice and sepsis (see SIRS criteria page 211)<br>#Do not continue Gentamicin beyond 3 - 4 days unless on the advice of an infection specialist. If you are unsure whether > 4 days is needed, contact an infection specialist.<br>*If eGFR < 20ml/minute/1.73m²: Piperacillin / Tazobactam IV 4.5 g 12 hourly (maximum)<br>*Alert Antibiotic - complete Alert form. |
| Post-operative intra-abdominal sepsis (laparotomy) | Piperacillin / tazobactam IV 4.5 g 8 hourly*<br>*If true penicillin / beta-lactam allergy:*<br>Contact microbiology<br>Total duration: Subject to regular clinical review and no more than 7 days in total. | Send pus samples (rather than swab) to microbiology.<br>Rationalise therapy based on microbiology results.<br>*If eGFR < 20ml/minute/1.73m²: Piperacillin / Tazobactam IV 4.5 g 12 hourly (maximum).<br>*Alert Antibiotic - complete Alert form. |
| *Clostridium difficile* infection | See flowchart page 239 | |

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| Table continued from previous page | | |
|---|---|---|
| **Infection** | **Antibiotic Therapy** | **Notes / Comments** |
| Gastroenteritis<br>(*Campylobacter spp., Salmonella spp., Shigella spp., viruses*) | Antibiotic therapy if invasive salmonella suspected (seek advice).<br>No antibiotics for *E coli* O157 (potentially harmful) or *Campylobacter* (no benefit). | Contact infectious diseases unit or microbiology for advice (Appendix 6 for contact details).<br>Avoid / review anti-motility agents (e.g. loperamide, opiates etc). |
| Spontaneous bacterial peritonitis<br>Chronic liver disease and ascites and peritoneal white cell count > 500/mm$^3$ or > 250 neutrophils/mm$^3$. | Co-amoxiclav IV 1.2 g 8 hourly<br>*If true penicillin / beta-lactam allergy*:<br>Ciprofloxacin* IV 400 mg 12 hourly or oral 500 mg 12 hourly<br>**and**<br>Vancomycin IV (dosing info page 266)<br>*Mild disease or oral continuation of treatment*:<br>Co-amoxiclav oral 625 mg 8 hourly<br>**or** *if penicillin / beta-lactam allergy:* contact microbiology / infectious diseases unit.<br>Total course duration 7 - 10 days (IV and oral). | See management of ascites page 56.<br>Send peritoneal aspirate in both blood culture bottles and universal container to microbiology.<br>If SBP and on prophylactic quinolone and beta-lactam allergy discuss with microbiology / infectious diseases unit.<br>*Ciprofloxacin QTc prolongation |
| *H. pylori* | See page 48 | |

See next page for Management of suspected *Clostridium difficile* infection (CDI)

# Management of suspected *Clostridium difficile* infection (CDI)

See next page for treatment of relapse.

Early (empirical) management of CDI may be life-saving. Management of CDI includes ensuring adequate hydration.

Patient with loose stools and either a history of recent antibiotic / hospitalisation (and no alternate diagnosis) or stool positive for *C. difficile* toxin.

↓

Ensure compliance with infection control guidelines and obtain stool for *C. difficile* toxin.

- **Monitor** frequency and severity of diarrhoea daily
- **Review and document** fluid, electrolytes and nutrition daily
- **Start** empiric treatment
- **Where possible:**
- **Stop / review / rationalise** non-Clostridial antimicrobials, opiates, gastric acid suppression
- **Stop** antimotility agents (e.g. loperamide)

- **Do** radiological assessment of abdomen if tenderness or distension
- **Consider** radiological assessment of the abdomen in absence of abdominal tenderness or distension **if** other severity markers are present (see below)

↓

**Assess severity of disease**

***Severity markers***: Colonic dilatation > 6 cm; WCC > 15 x $10^9$ cells/L; Creatinine > 1.5 x baseline; Temperature > 38.5$^{O}$ C; Immunosuppression

**Severity markers 0 - 1**

↓

**Non severe**

↓

**Metronidazole oral 400 mg three times daily for 10 - 14 days**

↓

If loose stools still continue after 5 days of metronidazole therapy or clinical condition worsens at any time

↓

**Switch to Vancomycin oral 125 mg four times daily for 10 - 14 days**

**Colonic dilation on its own or ≥ 2 Severity markers**

↓

**Severe**

↓

Consider surgical review

**Severe / Complicated**

For instance:

- Partial / complete ileus
- Systolic BP < 90 mmHg despite IV fluid resuscitation and /or
- Radiological evidence of severe disease colitis

↓

Surgical review and discuss with microbiology / infectious diseases unit

↓

**Vancomycin oral 125 mg four times daily for 10 - 14 days.**

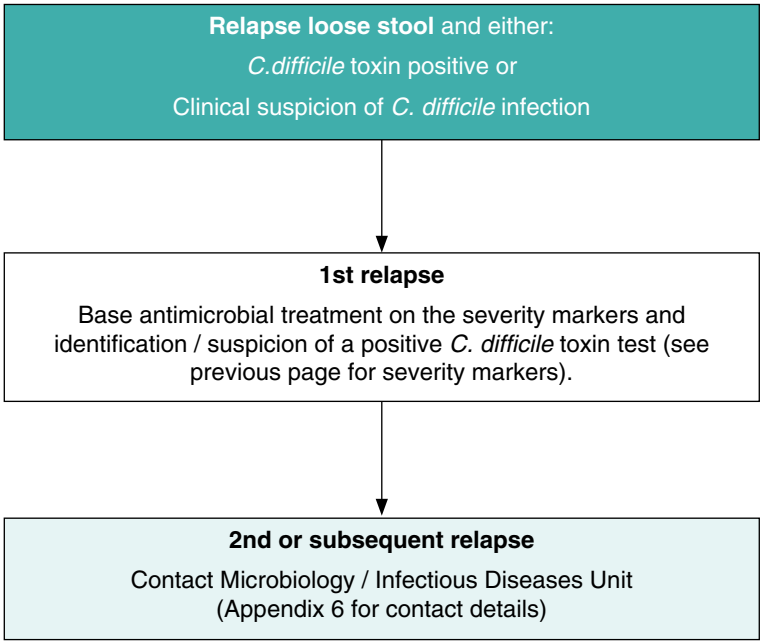
If ileus present then add in:

**Metronidazole IV 500 mg three times daily** and continue until it resolves.

If GI tract function is compromised, then discuss delivery options with microbiology / infectious diseases unit.

**Note**: If nil by mouth use IV formulation vancomycin via nasogastric tube

# Treatment of *Clostridium difficile* relapse



# Skin and soft tissue infections

- Likely organisms: *Streptococcus pyogenes* and *Staphylococcus aureus*
- Assess severity of infection. Document in patient's notes presence of:
  - Heat / erythema / induration / swelling (indicates severe infection if any 2 of these signs present).
  - Systemic Inflammatory Response Syndrome (SIRS) score (see page 211) indicates severe infection if SIRS > 2.

| Infection | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Mild cellulitis / erysipelas | Flucloxacillin oral 1 g 6 hourly<br>**or**<br>*If true penicillin / beta-lactam allergy:*<br>Doxycycline oral 100 mg 12 hourly<br>**or**<br>Clarithromycin* oral 500 mg 12 hourly<br>Total course duration 7 days. | If clinically clear cut or microbiologically proven Beta haemolytic Streptococcal infection (erysipelas) then treatment with oral Penicillin V 500 mg 6 hourly (monotherapy) is acceptable but review clinical response.<br>*Clarithromycin – serious drug interactions (see BNF Appendix 1) and QTc prolongation. |
| Moderate cellulitis / erysipelas (requiring IV therapy) | Flucloxacillin IV 1- 2 g 6 hourly<br>**or**<br>*If true penicillin / beta-lactam allergy*:<br>Vancomycin IV (dosing info page 266)<br>Total course duration (IV and oral): 10 days | If clinically clear cut or microbiologically proven Beta haemolytic Streptococcal infection (erysipelas) then treatment with Benzylpenicillin IV 1.2 g 6 hourly (monotherapy) is acceptable but review clinical response.<br>See IVOST protocol page 205 for appropriate time to change to oral therapy and switch options. |

Table continues on next page

| Skin and soft tissue infections (continued from previous page) | | |
|---|---|---|
| **Infection** | **Antibiotic Therapy** | **Notes / Comments** |
| Severe or rapidly spreading cellulitis / erysipelas or streptococcal toxic shock (non-drug user) | Flucloxacillin IV 2 g 4 - 6 hourly<br>**and**<br>Gentamicin* IV (dosing info page 262)<br>**and**<br>Clindamycin** IV 600 mg 6 hourly<br>If true penicillin / beta-lactam allergy:<br>Vancomycin IV (dosing info page 266)<br>**and**<br>Gentamicin IV (dosing info page 262)<br>**and**<br>Clindamycin** IV 600 mg 6 hourly<br>Total course duration usually 10 days (IV and oral). | If clinically clear cut or microbiologically proven Beta haemolytic Streptococcal infection (erysipelas) then add: Benzylpenicillin IV 1.2 g 6 hourly.<br>See IVOST protocol page 205 for appropriate time to change to oral therapy and switch options. If using Vancomycin or Gentamicin contact microbiology / infectious diseases unit for oral switch guidelines.<br>Consider referral to OPAT (see Appendix 6 for contact details)<br>*Do not continue Gentamicin beyond 3 - 4 days unless on the advice of an infection specialist. If you are unsure whether > 4 days is needed, contact an infection specialist.<br>**Alert antibiotic – complete Alert Form. |
| | | Table continues on next page |

| Skin and soft tissue infections (continued from previous page) | | |
|---|---|---|
| **Infection** | **Antibiotic Therapy** | **Notes / Comments** |
| Suspected necrotising fasciitis (non drug user or drug user) or any rapidly spreading or severe infection **in parenteral drug user** | Benzylpenicillin IV 2.4 g 6 hourly<br>and<br>Flucloxacillin IV 2 g 4 - 6 hourly<br>**and**<br>Gentamicin IV (dosing info page 262)<br>**and**<br>Clindamycin* IV 600 mg 6 hourly (up to 1200 mg 6 hourly)<br>Metronidazole IV 500 mg 8 hourly<br>*If MRSA suspected or if true penicillin / beta-lactam allergy:*<br>Treat as above **but** replace flucloxacillin and benzylpenicillin with:<br>Vancomycin IV (dosing info page 266)<br>Total course duration 10 - 14 days**. | Seek urgent surgical / orthopaedic review and advice from microbiology / infectious diseases unit.<br>*Clindamycin is an alert antibiotic. Complete alert form to obtain supply.<br>** At 48 hours consult microbiology / infectious diseases unit before discontinuing or switching from IV to oral. |
| Leg ulcers | Treat only if additional evidence of clinical infection* is present.<br>If antibiotic therapy is required treat as cellulitis and refer for specialist opinion following clinical review and if judged to be severe. | *Signs of clinical infection are:<br>Inflammation / redness / cellulitis with at least one of:<br>- Increased pain;<br>- Purulent exudate;<br>- Rapid deterioration of ulcer; or<br>- Pyrexia.<br>If no signs of clinical infection, antibiotics do not improve healing. Bacteria will always be present.<br>Diabetic foot ulcers require specialist podiatry / diabetes team assessment for evidence of deep seated (bone) infection (management of infection see page 245). |

Table continues on next page

| Skin and soft tissue infections (continued from previous page) | | |
|---|---|---|
| **Infection** | **Antibiotic Therapy** | **Notes / Comments** |
| Mild human or animal bite* or peri-anal soft tissue infection | Co-amoxiclav oral<br>625 mg 8 hourly<br>*If true penicillin / beta-lactam allergy*:<br>Doxycycline oral<br>100 mg 12 hourly<br>**and**<br>Metronidazole oral<br>400 mg 8 hourly<br>Total course duration 7 days. | Mixed organisms likely.<br>Only treat human bites if clinical signs of infection following skin puncture or if tendon / joint involvement.<br>*Antibiotic therapy is required if skin punctured in (non-human) animal bites even if no evidence of acute infection. |
| Severe infected human or animal bite or peri-anal infection | Co-amoxiclav IV<br>1.2 g 8 hourly<br>*If true penicillin / beta-lactam allergy*:<br>Metronidazole IV<br>500 mg 8 hourly<br>**and**<br>Clarithromycin* IV<br>500 mg 12 hourly<br>**and**<br>Gentamicin** IV (dosing info page 262)<br>Total course duration 10 days. | Mixed organisms likely.<br>*Clarithromycin - serious drug interactions (see BNF Appendix 1) / QTc prolongation.<br>**Do not continue Gentamicin beyond 3 - 4 days unless on the advice of microbiology / infectious diseases unit. |

# Bone and joint infection

- Discuss with on-call orthopaedic surgeon if underlying metal work or recent surgery.
- Assess for risk factors for MRSA.
- Where possible obtain synovial fluid / deep tissue for culture.

| Infection | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Native joint septic arthritis / Osteomyelitis | Flucloxacillin IV 2 g 6 hourly<br>**and**<br>Gentamicin* IV (dosing info page 262)<br>*If true penicillin / beta-lactam allergy*:<br>Vancomycin IV (dosing info page 266)<br>**and**<br>Gentamicin* IV (dosing info page 262)<br>Total course duration (IV/ oral) dependent on surgical intervention. Usually 4 - 6 weeks but discuss with microbiology / infectious diseases unit. | Obtain cultures (blood and synovial fluid) prior to antibiotics.<br>Infections usually due to Gram-positive organisms.<br>*Do not continue Gentamicin beyond 3 - 4 days unless on the advice of an infection specialist. If you are unsure whether > 4 days is needed, contact an infection specialist.<br>Rationalise therapy following culture results and following discussion with microbiology / infectious diseases unit. |
| Suspected prosthetic joint infection | Vancomycin IV (dosing info page 266)<br>**and**<br>Gentamicin* IV (dosing info page 262)<br>Seek advice from microbiology within 48 hours.<br>Total course duration variable, discuss with microbiology / infectious disease unit. | Commence antibiotic therapy following intra-operative specimens.<br>Rationalise therapy following culture results and following discussion with microbiology / infectious diseases unit.<br>*Do not continue Gentamicin beyond 3 - 4 days unless on advice of an infection specialist. If you are unsure whether > 4 days is needed, contact an infection specialist. |
| Diabetic foot osteomyelitis | Treatment as for septic arthritis / osteomyelitis as above **and add in:**<br>Metronidazole* oral 400 mg 8 hourly<br>Total course duration (IV / oral) dependent on surgical intervention. Usually minimum 6 weeks but discuss with microbiology / infectious diseases unit | See notes above regarding gentamicin. Assess vascularity and signs of neuropathy.<br>Refer to local diabetes team for general foot management.<br>*Prolonged metronidazole associated with neuropathy. Discuss options with microbiology |

# Central nervous system infections

## Bacterial meningitis

- Meningitis is inflammation of the meninges. Symptoms of acute meningitis include: fever, headache, neck stiffness and photophobia. Always seek urgent advice from infectious diseases unit / microbiology. Discuss further management with infectious diseases unit on call at the Brownlee Centre, Gartnavel General Hospital. See Appendix 6 for contact details.
- The investigation of suspected meningitis must include:
  - Cerebrospinal fluid for gram stain, culture and polymerase chain reaction (PCR) for bacteria and viruses
  - Blood cultures
  - Throat swab
  - Clotted and EDTA blood for bacterial PCR
- Administer IV antibiotic therapy **urgently** on arrival in hospital and after blood cultures.
- Perform CT scan before lumbar puncture if: age > 60 years; seizures; reduced GCS or abnormal level of consciousness; CNS signs; immunosuppression.

**N.B.** contraindications to CT scan e.g. coagulopathy – discuss with radiology

- Duration of therapy dependent on aetiology: *N. meningitides* **7 days**; *S. pneumoniae* **14 days**; *L. monocytogenes* **21 days**, Herpes simplex / Varicella zoster viruses encephalitis IV therapy for **14 - 21** days.

**For treatment see table on next page**

| Bacterial meningitis | Treatment | Notes / Comments |
|---|---|---|
| Age < 50 years and Listeria **not** suspected[#] | Ceftriaxone* IV 2 g 12 hourly<br>**and**<br>Dexamethasone** IV 10 mg 6 hourly (for 4 days)<br>*or if true, life-threatening penicillin / beta-lactam allergy:*<br>Chloramphenicol IV 1 g 6 hourly **and** seek urgent advice from microbiology / infectious diseases unit<br>**and**<br>Dexamethasone** IV 10 mg 6 hourly (for 4 days)<br>Total course duration: Dependent on aetiology (see previous page). | Discuss all cases of suspected meningitis with infectious disease unit / microbiology (Appendix 6 for contact details).<br>[#]*Listeria* meningitis suspected in patients:<br>• > 50 years<br>• Immunosuppressed<br>• Pregnant<br>• Alcohol excess and liver disease<br>*Ceftriaxone:<br>• Alert antibiotic – complete Alert Form.<br>• Must not be mixed with calcium-containing solutions, and must not be given to any patient simultaneously with calcium-containing solutions – even via different infusion lines.<br>**Dexamethasone – stop if meningitis is non-bacterial. |
| Age ≥ 50 years or if *Listeria* meningitis[#] suspected | Ceftriaxone* IV 2 g 12 hourly<br>**and**<br>Dexamethasone** IV 10 mg 6 hourly (for 4 days)<br>**and**<br>Amoxicillin IV 2 g 4 hourly<br>*If true, life-threatening penicillin / beta-lactam allergy*<br>Chloramphenicol IV 1 g 6 hourly **and** seek urgent advice from microbiology / infectious diseases unit<br>**and**<br>Vancomycin IV (dosing info page 266)<br>**and**<br>Dexamethasone** IV 10 mg 6 hourly (for 4 days)<br>Total course duration: Dependent on aetiology (see previous page). | |

*Continues on next page*

## Meningitis Contacts

- All suspected cases of meningococcal disease are notified to the NHSGGC Board, Public Health Protection Unit (see Appendix 6 for contact detail)
- Specialists in Communicable Disease will identify close family and friends of the patient who may require antibiotic prophylaxis.
- This should be given as soon as possible (ideally within 24 hours) after diagnosis of the index case.

| Meningitis Contact Prophylaxis | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Oral therapy (whenever possible) | Ciprofloxacin oral 500 mg as a single dose | Ciprofloxacin has an unpredictable effect on epilepsy but is preferred to rifampicin if the patient is on phenytoin. Ciprofloxacin is also the recommended option in pregnancy.<br>Ciprofloxacin is unlicensed for this purpose.<br>See BNF for children's doses.<br>**N.B**. Ciprofloxacin QTc prolongation. |
| When oral therapy not appropriate | Ceftriaxone* 250 mg IM as a single dose | *Ceftriaxone:<br>• Is an Alert antibiotic – complete Alert Form.<br>• It must not be mixed with calcium-containing solutions, and must not be given to any patient simultaneously with calcium-containing solutions – even via different infusion lines. |

*Continues on next page*

# Brain abscess

- Perform blood cultures.
- Discuss treatment and duration with neurosurgery and microbiology / infectious diseases unit.

**Potential source:**

- Sinus (*Strep milleri, Pneumococcus, H. influenzae*)
- Middle ear (mixed aerobes and anaerobes)
- Post traumatic (*Staph aureus* or mixed infections)
- Blood stream, endocarditis (*Staph* and *Strep* species)

| Infection | Antibiotic Therapy | Notes / Comments |
|---|---|---|
| Upper respiratory tract source (sinus and middle ear) | Ceftriaxone* IV 2 g 12 hourly<br>**and**<br>Metronidazole IV 500 mg 8 hourly<br><br>Total course duration – discuss with neurology or microbiology / infectious diseases unit.<br>*If true penicillin / beta-lactam allergy*: contact microbiology / infectious diseases unit for advice (Appendix 6 for contact details). | *Ceftriaxone:<br>• Is an Alert antibiotic - complete Alert Form.<br>• Must not be mixed with calcium-containing solutions, and must not be given to any patient simultaneously with calcium-containing solutions – even via different infusion lines. |
| Post traumatic or blood stream source | **As above and add:**<br>Flucloxacillin IV 2 g 4 hourly<br>*If true penicillin / beta-lactam allergy*: contact microbiology / infectious diseases unit for advice (Appendix 6 for contact details).<br>Total course duration – discuss with neurology or microbiology / infectious diseases unit. | |

# Viral infections

## Viral Encephalitis

- Encephalitis is inflammation of the parenchyma of the brain. It is often associated with meningitis (meningoencephalitis).
- Symptoms include fever and headache with signs of cerebral involvement – fits, altered level of consciousness, confusion, personality change, focal neurological changes e.g. cranial nerve deficits.
- Herpes Simplex Virus (HSV) is the commonest cause of sporadic viral encephalitis. However in many cases no aetiological agent is identified.
- Treatment should be started with IV Aciclovir (see table below)
- Perform CT scan before lumbar puncture
- Send CSF for viral PCR as well as microbiology and biochemistry
- In the first 72 hours after the onset of HSV encephalitis, CSF PCR may be negative; repeat LP advised if the diagnosis is suspected

Duration of treatment for confirmed HSV encephalitis is at least 14 days with a second CSF sample for PCR advised after 14 days of treatment. If the HSV PCR remains positive continued treatment is recommended. Discuss with infectious deseases unit / virology

| Infection | Treatment | Notes / Comments |
|---|---|---|
| Possible viral encephalitis | Aciclovir IV 10 mg/kg 8 hourly. Adjust dose in renal impairment – see comments section.<br>Total course duration 14 - 21 days (IV only). | Renal impairment dosing (CrCl equation on page 260) :<br>CrCl 25 - 50 ml/minute: 10 mg/kg 12 hourly<br>CrCl 10 - 25 ml/minute: 10 mg/kg 24 hourly<br>CrCl < 10 ml/minute: See Summary of Product Characteristics (www.medicines.org.uk) |
| Herpes simplex | Aciclovir oral 200 mg five times daily<br>In some patients*:<br>Aciclovir oral 400 mg five times daily or consider IV administration 5 mg/kg 8 hourly<br>Adjust dose in renal impairment – see BNF for details.<br>Total course duration 5 days. | *Consider higher dose or IV administration if:<br>• severely immunocompromised or<br>• reduced enteral absorption. |

Table continues on next page

| Viral infections (continued from previous page) | | |
|---|---|---|
| **Infection** | **Treatment** | **Notes / Comments** |
| Varicella / herpes zoster | If < 48 hours after the onset of a rash:<br>Aciclovir oral 800 mg five times daily **or** Aciclovir IV* 10 mg/kg 8 hourly<br>**or**<br>Valaciclovir oral 1 g 8 hourly<br>For both agents adjust dose in renal impairment – see BNF for details.<br>Total course duration 7 days. | *Consider IV administration if:<br>• severely immunocompromised<br>or<br>• reduced enteral absorption. |
| Viral meningitis | | In general no specific antiviral treatment is recommended. Discuss with infectious diseases unit / virology |

# Genito-urinary (GU) infections

**Note:** For specialist advice and contact tracing following the diagnosis / suspicion of a sexually transmitted infection call **0141 211 8646** (Mon - Fri 09:00 - 16.30). Refer to any Sandyford hub on a "walk in" basis if: acute symptomatic suspected sexually transmitted infection including genital and rectal discharge or pain or male dysuria, acute genital ulceration, pelvic pain, acute symptomatic syphilis. Consultant GUM referral at Sandyford Central / Sandyford Renfrewshire for on-going management if: recurrent vaginal discharge / candida, recurrent herpes, non-responding warts, positive syphilis serology. *Any sexually transmitted disease occurring in pregnancy requires specialist referral. Tetracyclines and quinolones are contraindicated in pregnancy.*

| Infections | Treatment | Notes / Comments |
|---|---|---|
| Sexually transmitted infections (non-severe) | Contact GU medicines, Sandyford Initiative (Appendix 6 for contact details) for management advice and partner notification | Infections include:<br>chlamydia, gonorrhoea, genital herpes, *Trichomonas*, vaginosis, genital warts, non-severe pelvic inflammatory disease. |
| Gonorrhoea | Refer to Sandyford for specialist assessment, parenteral management and partner notification. Test and treat partners also. | Usually presents with genital or rectal discharge. May cause epididymitis; > 50% now quinolone resistant and oral cefixime no longer recommended due to fall in susceptibility. |
| Non-gonococcal urethritis | Treat as per Chlamydia (below) | Characterised in men by dysuria and mucoid / mucopurulent urethral discharge |
| *Chlamydia trachomatis* | Azithromycin oral 1 g stat (1 hour before or 2 hours after food) as a single dose<br>**or**<br>Doxycycline oral 100 mg 12 hourly for 7 days. | Samples should be taken before treatment. Patients with symptoms, i.e. pelvic pain in women, scrotal pain or urethral discharge in men, refer within 2 - 3 days. Test and treat partners. |
| Genital Herpes | Aciclovir oral 200 mg five times daily for 5 days. | |

Table continues on next page

| Genito-urinary infections (continued from previous page) | | |
|---|---|---|
| **Infections** | **Treatment** | **Notes / Comments** |
| Acute severe Pelvic Inflammatory Disease (PID) | Ceftriaxone* IV 2 g daily (continue until 24 hours after clinical improvement)<br>**and**<br>Doxycycline oral 100 mg 12 hourly<br>**and**<br>Metronidazole oral 400 mg 12 hourly<br>Total course duration (of oral antibiotics) is 14 days.<br>*If true penicillin / beta-lactam allergy:* contact microbiology / infectious diseases unit or Sandyford for advice (Appendix 6 for contact details). | *Ceftriaxone:<br>• Is an Alert antibiotic – complete Alert Form.<br>• Must not be mixed with calcium-containing solutions and must not be given to any patient simultaneously with calcium-containing solutions – even via different infusion lines. |
| Syphilis | Refer all positive blood tests indicating "syphilis" to Sandyford Clinic (Appendix 6 for contact details).<br>Refer to the Brownlee centre if inpatient management required. | Recent resurgence of syphilis in Glasgow. Consider if new genital lesion(s) or widespread skin rash (usually including palms). |
| Vaginal candidiasis | Clotrimazole insert one 500 mg pessary at night as a single dose<br>**or**<br>Fluconazole oral 150 mg as a single dose. | Consider genital Herpes before making diagnosis of Candida infection. All topical and oral azoles give 80 - 95% cure. In pregnancy avoid oral azoles.<br>Refer to Sandyford if multiple attacks or not improving. |
| Bacterial vaginosis | Metronidazole oral 400 mg every 12 hours for 7 days<br>**or**<br>Metronidazole 0.75% vaginal gel insert applicatorful (5 g) at night for 5 days. | If minimal symptoms, no treatment required<br>Metronidazole 7 day treatment is slightly more effective than 2 g stat (BNF dose). Avoid 2 g stat dose in pregnancy. Topical treatment gives similar cure rates but is more expensive. |

Table continues on next page

| Genito-urinary infections (continued from previous page) | | |
|---|---|---|
| **Infections** | **Treatment** | **Notes / Comments** |
| Trichomoniasis | Metronidazole oral 400 mg every 12 hours for 5 days<br>**or**<br>Metronidazole oral 2 g as a single dose<br>**or**<br>Clotrimazole pessary 100 mg insert each night for 6 days. | Refer to GUM. Treat partners. In pregnancy avoid 2 g single dose metronidazole. Clotrimazole gives symptomatic relief, not cure. |
| Proctitis | | Rectal discharge, pain, constipation and tenesmus following unprotected receptive anal sex. Exclude gonorrhoea and lymphogranuloma venereum. Refer to Sandyford for proctoscopy. |
| Balanitis | | Usually settles with salt water bathing / avoidance of irritants. |
| Genital warts | Podophyllotoxin 0.15% cream self-applied 12 hourly 3 consecutive days per week for 4 - 6 weeks. | Avoid in pregnancy. |

## Invasive candidiasis in non-haemato-oncology adult patients

See guideline on StaffNet, Clinical Guideline Electronic Resource Directory, and search in 'Infections' section.

# HIV infection in hospital

- Contact Brownlee Centre, Gartnavel General Hospital (see Appendix 6 for contact details) if HIV is suspected in an inpatient or patient is known HIV positive.
- Ensure uninterrupted supply of anti-retroviral therapy. The patient should have their own supply of anti-retroviral therapy. Otherwise contact Gartnavel General Hospital Pharmacy (see Appendix 6 for contact details).
- Drug Interactions are common. Please contact HIV pharmacist (see Appendix 6 for contact details).

## Post-exposure Prophylaxis (PEP)

See guideline titled 'NHSGGC Management of Occupational and Non Occupational Exposures to BBV' on StaffNet, Clinical Guideline Electronic Resource Directory, and search in 'Infections' section.

Assess recipients of blood borne virus exposure urgently, as soon as possible after injury. Ideally PEP should be given within 2 hours of injury but is still beneficial beyond this time.

### General management:

- Assess the injury.
- Administer first aid.
- Assess the source risk and need for blood borne virus testing in conjunction with the index patients clinical team.
- Check for potential drug interactions. Contact pharmacy (see Appendix 6 for contact details).
- Contact the Brownlee Centre, Gartnavel General Hospital (see Appendix 6 for contact details) for all patients who are assessed as requiring PEP or if there is uncertainty.
- Obtain post-exposure prophylaxis medication (PEP packs) through A&E or pharmacy.
- For patients with sexual exposure to HIV, contact the Sexual Health Service at the Sandyford Centre (see Appendix 6 for contact details).
- HIV counselling and testing is provided at the Brownlee Centre, Sandyford Central and multiple Sandyford Hubs in NHSGGC (see www.sandyford.org for details).
- Refer all incidents to occupational health.

# Patients with absent or non-functioning spleen

- A non-functioning spleen may be due to blood dyscrasia, coeliac disease, inflammatory bowel disease, bone marrow or stem cell transplant, dermatitis herpetiformis or may be congenital.
- Patients with absent or non-functioning spleen are at increased risk of overwhelming infection (particularly with *Streptococcus pneumoniae, Haemophilus influenzae, Neisseria meningitides*, influenza and malaria in travellers).

## General Management

Check immunisation history with patient, administer vaccinations appropriately (Table 2) and inform patient's GP.

**Table 1 – Vaccination schedules for splenectomy patients**

| Procedure | Time schedule for vaccinations |
|---|---|
| Planned splenectomy | *4 - 6 weeks pre-operatively.<br>If this is not possible, then 2 weeks pre-operatively. |
| Unplanned splenectomy | 2 weeks post-operatively (antibody response may be better). |
| Completion of radio- or chemotherapy | Delay vaccination for at least 3 months. |
| Bone marrow transplant | 9 - 12 months post transplant. |

**Table 2 – Vaccinations**

| Vaccinations | Notes / Comments |
|---|---|
| *Haemophilus influenzae* type b (Hib) | Adults who have been fully immunised with Hib /MenC as part of routine vaccination programme give:<br>Single one off dose (combined Hib/MenC vaccine) and followed 4 weeks later by MenACWY conjugate vaccine. |
| Meningococcal Group C conjugate (MenC) | |
| Influenza vaccine | Recommended yearly to all adult patients. |
| Pneumococcal vaccine | Give at same time as Hib/MenC vaccine.<br>For all patients re-immunisation is recommended every 5 years |

If immunisation unknown / cannot be clarified or for *further information see the Green Book via www.dh.gov.uk or British Committee for Standards in Haematology (www.bcshguidelines.com) or contact the immunology department.

### Antibiotic prophylaxis

**Amoxicillin oral 500 mg every 24 hours.**

*If true penicillin / beta-lactam allergy*:

**Erythromycin oral 500 mg every 24 hours.**

All patients with an absent or dysfunctional spleen should receive prophylactic antibiotics for at least 2 years, but ideally for life. Prophylactic antibiotics should be started immediately post surgery.

# Outpatient Parenteral Antibiotic Therapy (OPAT)

The OPAT service can provide IV antimicrobial therapy on an outpatient basis or at home for patients who require short or long-term IV therapy and who are otherwise suitable for home treatment. Patients may be considered from throughout Greater Glasgow and Clyde. Infections commonly managed via OPAT are shown below but any infections may be discussed and considered.

## Skin and soft tissue infection

Includes: cellulitis / wound infections / bursitis / infected bites / facial erysipelas. May be referred from emergency department or ward.

## Other complex infections

Usually inpatients are referred in conjunction with microbiology advice. Up to date U&Es, LFTs, FBC, CRP and microbiology results are required for all referrals:

- Osteomyelitis
- Septic arthritis
- Diabetic foot infections
- Infective endocarditis
- Meningitis
- Other infections can be discussed as required

The specialist team will assess patient suitability for OPAT and will agree a treatment regimen.

See Appendix 6 under Gartnavel General Hospital for OPAT contact details.

# MRSA Eradication Policy

- In newly recognised MRSA colonisation (MRSA isolated from the skin or mucous membrane), prescribe as follows (rule out any allergies first):
  - **NASAL mupirocin 2% applied to both nostrils 3 times daily for 5 days.** (Do not prescribe in pregnancy or lactation unless considered essential by the physician.)
  - **Hibiscrub Plus® used as soap in bath or shower daily for 5 days. Use also as shampoo 2 days out of 5.**
- Re-test patient at least two days after the end of the decolonisation regimen. The patient should no longer be considered colonised with MRSA when 2 repeat screens, taken every 3 days starting two days after the end of the decolonisation regimen, are negative.
- Contact infection control or microbiology if:
  - Patient has received two previous courses of the decolonisation regimen and is still testing positive.
  - MRSA is isolated from multiple sites, or those in whom colonisation is persistent or recurring.
  - Mupirocin resistant MRSA is isolated.

# Surgical Antibiotic Prophylaxis

The policy is based on SIGN 104 (July 2008) which outlines those surgical procedures requiring prophylactic antibiotics and how and when they should be administered.

Refer to surgical speciality guidelines at StaffNet, Clinical Guideline Electronic Resource Directory and search in 'Infections' section for specific agent(s) and regimens, including gentamicin prophylaxis guideline.

## General antibiotic prophylaxis prescribing guidance

- Check whether indication is appropriate. See tables on StaffNet for indication and antibiotic choice. Always discuss any complex individual prophylaxis issues with microbiology pre-operatively.
- Record antibiotic in the “once only” section of drug prescription form, not in the anaesthetic record.
- Administer a single dose of antibiotic(s). Optimum time is $\leq$ 60 minutes prior to skin incision (usually in anaesthetic room at induction of anaesthesia). If > 1 hour has elapsed, cover will be sub-optimal.
- In some circumstances a second dose may be required. If so always document the reason which may be:
  - >1.5 litre intra-operative blood loss in which case following fluid replacement, re-dose giving same dose for all agents except gentamicin (give only half the recommended prophylaxis dose) and teicoplanin (do not redose).
  - If surgery is prolonged then re-dose as per specific prophylaxis guideline
- MRSA: decolonise prior to procedure as per NHSGGC infection control guidelines and discuss with microbiology regarding antibiotic choice.
- Prophylactic gentamicin dosing is based on patient height and approximates to 3 mg/kg/ideal body weight, capped at 300 mg (see StaffNet for dosing table). This allows bolus administration in anaesthetic room. Avoid prophylactic gentamicin if eGFR < 10ml/minute/1.73m$^2$: seek advice on an alternative from microbiology.

## Post-operative intra-abdominal infection management

**Infection present prior to and following surgery**: When intra-abdominal surgery has been performed as part of the management of an infection episode (e.g. laparotomy for peritonitis), antibiotic therapy as per infection management guidelines should be followed.

**No infection suspected prior to surgery**: For suspected intra-abdominal sepsis following intra-abdominal surgery / laparoscopy (e.g. following routine or “cold” colorectal surgery) where gentamicin has been used within the prophylactic regime, give piperacillin and tazobactam, see page 237. If true penicillin / beta-lactam allergy discuss treatment options with microbiology.

For any other post-operative infection, seek advice from microbiology or the infectious diseases unit.

# Dosage regimens for antibiotics with narrow therapeutic ranges

**Height and weight conversion and maximum body weight for creatinine clearance estimation (MBW)**

| Maximum body weight table | | | |
|---|---|---|---|
| Height (feet/ inches) | Height (cm) | MBW (kg) (male) | MBW (kg) (female) |
| 4'8" | 142 | 49 | 43 |
| 4' 9" | 145 | 52 | 47 |
| 4' 10" | 147 | 54 | 49 |
| 4' 11" | 150 | 58 | 52 |
| 5' 0" | 152 | 60 | 55 |
| 5' 1" | 155 | 62 | 58 |
| 5' 2" | 158 | 66 | 60 |
| 5' 3" | 160 | 68 | 62 |
| 5' 4" | 163 | 71 | 66 |
| 5' 5" | 165 | 74 | 68 |
| 5' 6" | 168 | 77 | 71 |
| 5' 7" | 170 | 79 | 74 |
| 5' 8" | 173 | 82 | 77 |
| 5' 9" | 175 | 85 | 79 |
| 5' 10" | 178 | 88 | 82 |
| 5' 11" | 180 | 90 | 85 |
| 6' 0" | 183 | 94 | 88 |
| 6' 1" | 185 | 96 | 90 |
| 6' 2" | 188 | 98 | 94 |
| 6' 3" | 191 | 101 | 97 |
| 6' 4" | 193 | 104 | 99 |
| 6' 5" | 195 | 107 | 101 |
| 6' 6" | 198 | 109 | 105 |
| 6' 7" | 201 | 113 | 108 |
| 6' 8" | 203 | 115 | 110 |

| Weight conversion table | | |
|---|---|---|
| Stones | lb | kg |
| 5 | 0 | 32 |
| 5 | 7 | 35 |
| 6 | 0 | 38 |
| 6 | 7 | 41 |
| 7 | 0 | 45 |
| 7 | 7 | 48 |
| 8 | 0 | 51 |
| 8 | 7 | 54 |
| 9 | 0 | 57 |
| 9 | 7 | 60 |
| 10 | 0 | 64 |
| 10 | 7 | 67 |
| 11 | 0 | 70 |
| 11 | 7 | 73 |
| 12 | 0 | 76 |
| 12 | 7 | 80 |
| 13 | 0 | 83 |
| 13 | 7 | 86 |
| 14 | 0 | 89 |
| 14 | 7 | 92 |
| 15 | 0 | 95 |
| 15 | 7 | 99 |
| 16 | 0 | 102 |
| 16 | 7 | 105 |
| 17 | 0 | 108 |
| 18 | 0 | 115 |
| 19 | 0 | 121 |

### Estimation of creatinine clearance

The following 'Cockcroft Gault' equation can be used to estimate creatinine clearance (CrCl).

$$\text{CrCl (ml/minute)} = \frac{[140 - \text{age (years)}] \times \text{weight (kg)}}{\text{serum creatinine (micromol/L)}} \times 1.23 \text{ (male) OR } \times 1.04 \text{ (female)}$$

## Cautions!

- Use actual body weight (ABW) or maximum body weight (MBW), whichever is lower.
- Use 60 micromol/L if the creatinine concentration is < 60 micromol/L.
- This equation may overestimate CrCl in elderly or malnourished patients.
- **DO NOT USE eGFR**.

# Amikacin dosing guidelines *(For patients aged ≥ 16 years)*

**N.B.** See previous page for creatinine clearance (CrCl) and maximum body weight calculations.

| CrCl (ml/minute) | Dose | Alternative |
|---|---|---|
| 20 - 29 | 5.5 mg/kg 24 hourly | None |
| 30 - 49 | 6 mg/kg 24 hourly | None |
| 50 - 70 | 6 mg/kg 12 hourly | 12 mg/kg 24 hourly |
| > 70 | 7.5 mg/kg 12 hourly | 15 mg/kg 24 hourly |

### Target Concentrations

- Peak (1 hour post dose) 15 - 30 mg/L
- Trough (pre-dose) < 5 mg/L

**Alternative dosing:**

- Peak (1 hour post dose) > 35 mg/L
- Trough (pre-dose) < 2 mg/L

### Sampling Guidelines

- Check peaks (1 hour post dose) and troughs (end of dosage interval) within the first 48 hours of therapy and every 2 - 3 days thereafter.
- Dose requirements will change if renal function alters – check creatinine concentration and eGFR daily.
- **Please** record the **exact times** of all **doses and samples** on the request form and the sample times on the sample tubes.
- Seek advice from pharmacy or microbiology if you are unsure how to interpret the result.

# Tobramycin dosing guidelines *(For patients aged ≥ 16 years)*

## Patients with Cystic Fibrosis (CF)

Check the ward list for the patient's normal dose (Gartnavel General Hospital) and check a peak (1 hour after dose) and a trough (end of dosage interval) within the first 24 - 36 hours of therapy. The target peak is 8 -12 mg/L and trough < 1 mg/L.

**Or**

for **new** CF patients, use the ward guidelines to calculate the initial dosage regimen. Sampling guidelines as above. Seek advice from pharmacy or microbiology if you are unsure how to interpret the result.

## Non-CF patients

To calculate tobramycin dose use the gentamicin dosing guideline on the next page.

# Gentamicin dosing guidelines *(For patients aged ≥ 16 years)*

*This guideline does not apply to:*

- Patients treated in renal units or receiving haemodialysis or haemofiltration
- Major burns
- Ascites
- Cystic fibrosis
- Synergistic use of gentamicin

*Refer to local guidelines for managing these patients.*

**Contra-indications:** Hypersensitivity, myasthenia gravis

**Cautions:**

- Chronic Kidney Disease Stage 4/5, ≥ 50% increase in serum creatinine or oliguria for > 6 hours in the past 48 hours
  - If gentamicin is clinically indicated, give one dose as per guidance and check with microbiology, an infection specialist or pharmacy before giving a second dose.
- Avoid in decompensated liver disease (jaundice, ascites, encephalopathy, variceal bleeding or hepatorenal syndrome).
- Avoid co-administration with neurotoxic or nephrotoxic agents, e.g. neuromuscular blockers, non-steroidal anti-inflammatory drugs, Angiotensin Converting Enzyme Inhibitors; potent diuretics; other aminoglycosides (see www.medicines.org.uk).

## Prescribing and documentation

- Use the gentamicin prescribing and monitoring chart to prescribe and record all doses and concentration measurements.
- The following pages outline 3 steps, from calculating and prescribing the first dose to monitoring and assessing gentamicin therapy.

### Step 1: Calculate, prescribe and administer the first dose

- To reduce the risk of mortality, commence gentamicin administration within 1 hour of recognising sepsis.
- *If creatinine is known* - use the online calculator on StaffNet, Clinical Info section or the table on the next page (only if the online calculator is not available). The dose amount and dosage interval are based on estimated creatinine clearance (see page 260) and **actual** body weight (ABW). **Do not use eGFR.**
- *If creatinine is not known* - give 5 mg/kg **actual** body weight (maximum 400 mg) or, if CKD 5, give 2.5 mg/kg (maximum 180 mg).
- Give the recommended dose by infusion in 100 ml sodium chloride 0.9% over 30 minutes.

*Continues on next page*

Step 1 continued from previous page

**Table 1: Initial GENTAMICIN doses and dose intervals**

| Actual body weight → / Creat Cl (ml/minute)↓ | 40 - 49 kg | 50 - 59 kg | 60 - 69 kg | 70 - 80 kg | > 80 kg |
|---|---|---|---|---|---|
| < 21 | 2.5 mg/kg (max 180 mg) then take a sample after 24 hours | | | | |
| 21 – 30 | 180 mg 48 hourly | 200 mg 48 hourly | 240 mg 48 hourly | 240 mg 48 hourly | 260 mg 48 hourly |
| 31 – 40 | 200 mg 48 hourly | 240 mg 48 hourly | 280 mg 48 hourly | 300 mg 48 hourly | 320 mg 48 hourly |
| 41 – 50 | 240 mg 48 hourly | 280 mg 48 hourly | 320 mg 48 hourly | 360 mg 48 hourly | 400 mg 48 hourly |
| 51 – 60 | 200 mg 24 hourly | 240 mg 24 hourly | 280 mg 24 hourly | 300 mg 24 hourly | 320 mg 24 hourly |
| > 60 | 240 mg 24 hourly | 280 mg 24 hourly | 320 mg 24 hourly | 360 mg 24 hourly | 400 mg 24 hourly |

**Note:** If the patient weighs < 40 kg and CrCl is ≥ 21 ml/minute, give a single dose of 5 mg/kg then take a sample 6 – 14 hours after the dose. If the patient weighs > 150 kg please contact pharmacy or the local antimicrobial pharmacist (see Appendix 6 for contact details).

## Step 2: Monitor creatinine and gentamicin concentrations and reassess the dosage regimen

Concentrations are meaningless unless the dose and sample time are recorded accurately

**If CrCl is ≥ 21 ml/minute**

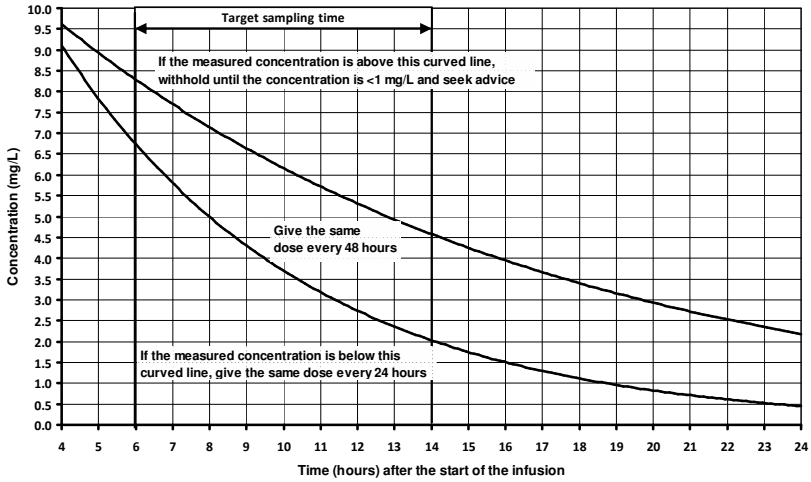
- Take a blood sample 6 - 14 hours after the start of the first gentamicin infusion.
- Record the exact time of all gentamicin samples on the gentamicin prescribing chart **and** on the sample request form.
- Record the serum concentration on the gentamicin prescribing chart.
- Plot the concentration measurement on the graph. This will indicate one of 3 options: 1) continue the present dosage regimen; 2) adjust the dosage interval; 3) withhold and resample after 24 hours.

**If CrCl is < 21 ml/minute**

- Take a blood sample 24 hours after the start of the first gentamicin infusion
- Record the exact time of all gentamicin samples using the gentamicin prescribing chart **and** on the sample request form.
- *If therapy is to continue*, take additional blood samples at least every 24 hours and give a further dose once the measured concentration is < 1 mg/L

*Gentamicin graph on next page*

**Step 2** continued from previous page




**General points**

- Document the action taken in the medical notes and on the gentamicin prescribing chart.
- Undertake pre-prescribing checks to assess the risk of renal toxicity and ototoxicity (see next page). Prescribe the next dose as appropriate.
- Seek advice from pharmacy or microbiology if you are unsure how to interpret the result or if the concentrations are very low or very high. Doses up to 600 mg may be required for some patients.
- If a blood sample is not taken, is lost or is taken at wrong time and if there is any concern about the patient's renal function, take a sample at 20 - 24 hours and wait for the result before giving the next dose. Otherwise, take a blood sample after the next dose.
-

**If the measured concentration is unexpectedly HIGH or LOW, consider the following:**

- Were dose and sample times recorded accurately?
- Was the correct dose administered?
- Was the sample taken from the line used to administer the drug?
- Was the sample taken during drug administration?
- Has renal function declined or improved?
- Does the patient have oedema or ascites?
- Is the patient severely underweight or overweight?

If in doubt, take another sample before re-prescribing and / or contact pharmacy for advice

*Step 3 continues on the next page*

### Step 3: Assess daily: the ongoing need for gentamicin and signs of toxicity

- Take a further sample 6 - 14 hours after the dose, at least every 2 days.
- If the concentration is unexpectedly high or if renal function alters, daily sampling may be necessary.
- To minimise the risk of toxicity, duration of treatment should normally be limited to 3 days. All gentamicin prescriptions that continue beyond 3 - 4 days of treatment **must** be discussed with an infection specialist. Consider changing to an oral alternative - refer to the IV to Oral switch policy, on page 205.

### Renal Toxicity

- Monitor creatinine daily. Seek advice if renal function is unstable (e.g. a change in creatinine of > 15 - 20%).
- Signs of renal toxicity include an increase in creatinine or decrease in urine output / oliguria.
- Consider an alternative agent if creatinine is rising or the patient becomes oliguric.

### Ototoxicity

- Ototoxicity secondary to gentamicin is independent of drug concentration. It is suggested by any of the following: new tinnitus, dizziness, poor balance, hearing loss or oscillating vision.
- Toxicity is associated with prolonged aminoglycoside use (usually > 10 days but may be > 3 days) and is secondary to drug accumulation within the inner ear.
- Stop treatment if ototoxicity is suspected and refer to a microbiology / infection specialist for advice on future therapy
- If gentamicin continues for > 7 days, suggest referring to audiology for assessment.

# Vancomycin dosing guidelines *(For patients aged ≥ 16 years)*

## General points

- Continuous infusion of vancomycin is preferred for patients with severe or deep-seated infections (e.g. pneumonia, endocarditis, bone and joint infections).
- These guidelines **do not apply** to patients in Renal Units, on haemodialysis or on haemofiltration.
- *Contra-indications*: hypersensitivity
- *Cautions*: Co-administration with potentially nephrotoxic agents (amphotericin, potent diuretics, NSAIDs, aminoglycosides, ACE inhibitors – see www.medicines.org.uk). Avoid in patients with previous hearing loss. To avoid the risk of "red-neck / red-man syndrome", pain or muscle spasm, administer no faster than 500 mg/hour.

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## A. Intermittent 'Pulsed' infusion **(if continuous infusion is not practical)**

### Prescribing and documentation

Refer to hospital site policy regarding how to prescribe vancomycin and where to record doses and concentration measurements.

### Step 1: Prescribe the loading dose and maintenance dosage regimen

- To reduce the risk of mortality, commence vancomycin administration within 1 hour of recognising sepsis.
- *If creatinine is known* – use the online calculator on StaffNet, Clinical Info section. If it is not available, use the Loading and Maintenance Infusion tables below. The dose amount and dosage interval are based on estimated CrCl (see page 260) and actual body weight (ABW). **Do not use eGFR.**
- *If creatinine is not known* – calculate the single loading infusion dose using actual body weight, prescribe and administer. Calculate the maintenance dose once creatinine is available.

**Table 1: Vancomycin LOADING infusion**

| Actual body weight | Dose amount | Volume of sodium chloride (0.9%) * | Duration of infusion |
|---|---|---|---|
| < 40 kg | 750 mg | 250 ml | 90 minutes |
| 40 – 59 kg | 1000 mg | 250 ml | 2 hours |
| 60 – 90 kg | 1500 mg | 500 ml | 3 hours |
| > 90 kg | 2000 mg | 500 ml | 4 hours |

* Glucose 5% may be used in patients with sodium restriction.

*Table 2: Vancomycin maintenance intermittent (pulsed) infusion continued on next page*

**Vancomycin maintenance intermittent (pulsed) infusion regimen**

Give the first maintenance infusion 12, 24 or 48 hours after the loading infusion according to the dose interval provided by the online calculator or the table below.

**Table 2: Vancomycin maintenance intermittent (pulsed) dosing regimen**

| CrCl (ml/minute) | Dose amount | Volume of sodium chloride (0.9%)* | Dose interval |
|---|---|---|---|
| < 20 | 500 mg over 1 hour | 250 ml | 48 hours |
| 20 - 29 | 500 mg over 1 hour | 250 ml | 24 hours |
| 30 - 39 | 750 mg over 1.5 hours | 250 ml | 24 hours |
| 40 - 54 | 500 mg over 1 hour | 250 ml | 12 hours |
| 55 - 74 | 750 mg over 1.5 hours | 250 ml | 12 hours |
| 75 - 89 | 1000 mg over 2 hours | 250 ml | 12 hours |
| 90 - 110 | 1250 mg over 2.5 hours | 250 ml | 12 hours |
| > 110 | 1500 mg over 3 hours | 500 ml | 12 hours |

* Glucose 5% may be used in patients with sodium restriction.

**N.B.** The daily dose can be split into 3 equal doses and given 8 hourly to produce higher troughs. For example, 1500 mg 12 hourly could be prescribed as 1000 mg 8 hourly and 750 mg 12 hourly as 500 mg 8 hourly.

## Step 2: Monitor vancomycin concentration and reassess the dosage regimen

Concentrations are meaningless unless the dose and sample time are recorded accurately

- Take a trough sample (pre-dose) within 48 hours of starting therapy then every 2 - 3 days, or daily if the patient has unstable renal function. Monitor creatinine daily.
- Record the exact time of all vancomycin samples on the vancomycin chart **and** on the sample request form.
- If renal function is stable, give the next dose before the result is available. If renal function is deteriorating, withhold until the result is available then follow the advice below.
- **Target trough concentration range: 10 – 20 mg/L**
- If the patient is **seriously ill** (severe or deep-seated infections), the target range is 15 – 20 mg/L (see table 3 on the next page).
- If the patient is failing to respond, seek advice from microbiology or an infection specialist.

**Adjustment of vancomycin dosage regimen (see table 3, next page)**

- Always check that the dosage history and sampling time are appropriate before interpreting the result.
- Seek advice from pharmacy or microbiology if you need help to interpret the result.

*If the measured concentration is unexpectedly HIGH or LOW, consider the following:*

- Were dose and sample times recorded accurately?
- Was the correct dose administered?

*Continues on next page*

*Continued from previous page - If the measured concentration is unexpectedly HIGH or LOW*

- Was the sample taken from the line used to administer the drug?
- Was the sample taken during drug administration?
- Has renal function declined or improved?
- Does the patient have oedema or ascites?
- Is the patient severely underweight or overweight?

**Table 3: Adjustment of vancomycin dosage regimen – intermittent 'pulsed' infusion**

| Vancomycin concentration | Suggested dose change |
|---|---|
| < 10 mg/L | Increase the dose by 50% and consider reducing the dosage interval. **Always seek advice** if you are unsure or if the current dose is > 2500 mg daily.* |
| 10 – 15 mg/L | If the patient is responding, maintain the present dosage regimen.<br>If the patient is seriously ill, consider increasing the dose amount or reducing the dosage interval to achieve a trough of 15 – 20 mg/L. |
| 15 – 20 mg/L | Maintain the present dosage regimen |
| > 20 mg/L | Stop until < 20 mg/L then seek advice |

* If daily doses above 4 grams are required, please ensure pharmacy have been contacted for advice.

**If in doubt, take another sample before modifying the dosage regimen and / or contact pharmacy for advice**

## General points

- Record the exact times of all measured concentrations on the vancomycin chart. If the dosage regimen needs to be changed, discontinue the present dose and prescribe a new dosage regimen.
- Document the action taken in the medical notes.
- Undertake pre-prescribing checks (see below) to assess the risk of toxicity.
- Review the need for vancomycin daily.

*Continues on next page*

**Toxicity**

- Monitor creatinine daily. Seek advice if renal function is unstable (e.g. a change in creatinine of > 15 - 20%).
- Signs of renal toxicity include an increase in creatinine or decrease in urine output / oliguria.
- Consider an alternative agent if creatinine is rising or the patient becomes oliguric.
- Vancomycin may increase the risk of aminoglycoside-induced ototoxicity.

*Guidance on vancomycin administration by continuous infusion on the next page*

## B. Vancomycin continuous infusion

### Step 1: Prescribe the loading dose and maintenance dosage regimen

- To reduce the risk of mortality, commence vancomycin administration within 1 hour of recognising sepsis.
- *If creatinine is known* – use the online calculator on StaffNet, Clinical Info section. If it is not available, use the Loading and Maintenance Infusion tables below. The dose amount and dosage interval are based on estimated creatinine clearance (see page 260) and **actual** body weight (ABW). **Do not use eGFR**.
- *If creatinine is not known* – calculate the single loading infusion dose using actual body weight, prescribe and administer. Calculate the maintenance dose once creatinine is available.

**Table 4: Vancomycin LOADING infusion**

| Actual body weight | Dose amount | Volume of sodium chloride (0.9%) * | Duration of infusion |
|---|---|---|---|
| < 40 kg | 750 mg | 250 ml | 90 minutes |
| 40 – 59 kg | 1000 mg | 250 ml | 2 hours |
| 60 – 90 kg | 1500 mg | 500 ml | 3 hours |
| > 90 kg | 2000 mg | 500 ml | 4 hours |

* Glucose 5% may be used in patients with sodium restriction.

### Vancomycin maintenance continuous infusion regimen

Start the continuous infusion **immediately** after the loading infusion is complete.

**Table 5: Vancomycin maintenance continuous dosing regimen**

| CrCl (mL/minute) | Daily dose | Dose for continuous infusion over 12 hours |
|---|---|---|
| < 20 | Use pulsed infusion or follow Renal Unit guidelines | |
| 20 - 29 | 500 mg | 250 mg |
| 30 - 39 | 750 mg | 375 mg |
| 40 - 54 | 1000 mg | 500 mg |
| 55 - 74 | 1500 mg | 750 mg |
| 75 - 89 | 2000 mg | 1000 mg |
| 90 - 110 | 2500 mg | 1250 mg |
| > 110 | 3000 mg | 1500 mg |

Dilute doses up to 1250 mg in 250 ml sodium chloride (0.9%) and doses above 1250 mg and up to 2000 mg in 500 ml sodium chloride 0.9%. Glucose 5% may be used in patients with sodium restriction.

*Step 2: Vancomycin continuous infusion continues on the next page*

Continued from previous page

## Step 2: Monitor vancomycin concentration and reassess the continuous infusion dose

**Concentrations are meaningless unless the dose and sample time are recorded accurately**

- Take a sample 12 – 24 hours after starting the continuous infusion then every 1 – 2 days or daily if the patient has unstable renal function. Monitor creatinine daily.
- Record the exact time of all vancomycin samples on the sample request form.
- If renal function is stable, give the next dose before the result is available. If renal function is deteriorating, withhold until the result is available then follow the advice on the table below.
- **Target steady state concentration range: 15 – 25 mg/L**. If the patient is **seriously ill (severe or deep-seated infections), the target range is 20 – 25 mg/L**
- If the patient is failing to respond, seek advice from microbiology or an infection specialist.

### Adjustment of vancomycin continuous infusion regimen

- Always check that the dosage history and sampling time are appropriate before interpreting the result.
- Seek advice from pharmacy or microbiology if you need help to interpret the result.

*If the measured concentration is unexpectedly HIGH or LOW, consider the following:*

- Were dose and sample times recorded accurately?
- Was the correct dose administered?
- Was the sample taken from the line used to administer the drug?
- Has renal function declined or improved?
- Does the patient have oedema or ascites?
- Is the patient severely underweight or overweight?

**Table 6: Adjustment of vancomycin dosage regimen – continuous infusion**

| Vancomycin concentration | Suggested dose change |
|---|---|
| < 15 mg/L | Increase the 12 hourly dose by 250 mg |
| 15 - 25 mg/L | If the patient is responding, maintain the present dosage regimen.<br>If the patient is seriously ill, consider increasing the dose amount to achieve a steady state level of 20 – 25 mg/L. |
| 26 - 30 mg/L | Decrease the 12 hourly dose by 250 mg |
| > 30 mg/L | Stop until < 25 mg/L then restart at a lower dose |

**If in doubt, take another sample before modifying the dosage regimen and/or contact pharmacy for advice**

*Continues on the next page*

### General points

- Record the exact times of all measured concentrations on the monitoring chart. If the dosage regimen needs to be changed, discontinue the present dose and prescribe a new dose.
- Document the action taken in the medical notes.
- Undertake pre-prescribing checks (see below) to assess the risk of toxicity.
- Review the need for vancomycin daily.

### Toxicity

- Monitor creatinine daily. Seek advice if renal function is unstable (e.g. a change in creatinine of > 15-20%).
- Signs of renal toxicity include an increase in creatinine or decrease in urine output / oliguria.
- Consider an alternative agent if creatinine is rising or the patient becomes oliguric.
- Vancomycin may increase the risk of aminoglycoside induced ototoxicity.

# Teicoplanin dosing guidelines *(For patients aged ≥ 16 years)*

Use vancomycin in renal replacement therapy.

## Teicoplanin dosing

| Renal Function (CrCl) | Weight (kg) | Teicoplanin Dose (IV / IM) |
|---|---|---|
| > 60 ml/minute | < 85 | 400 mg 12 hourly for 3 doses,<br>*then* 400 mg once daily |
| | > 85 | 6 mg/kg 12 hourly for 3 doses,<br>*then* 6 mg/kg once daily |
| 40 - 60 ml/minute | < 85 | 400 mg 12 hourly for 3 doses,<br>*then* 400 mg once daily for 2 days,<br>*then* 200 mg once daily or 400 mg on alternate days |
| | > 85 | 6 mg/kg 12 hourly for 3 doses,<br>*then* 6 mg/kg once daily for 2 days,<br>*then* 3 mg/kg once daily or 6 mg/kg on alternate days |
| < 40 ml/minute | < 85 | 400 mg 12 hourly for 3 doses,<br>*then* 400 mg once daily for 2 days,<br>*then* 400 mg every third day |
| | > 85 | 6 mg/kg 12 hourly for 3 doses,<br>*then* 6 mg/kg once daily for 2 days,<br>*then* 6 mg/kg every third day |

**N.B**. In deep-seated infections (e.g. endocarditis, bone and joint infections) seek advice from microbiology or infectious diseases department. Aim for a trough concentration of 20 - 30 mg/L.

Section 9

# Endocrine System

# Management of Diabetic Ketoacidosis (DKA)

**Aim:** To improve the acute management of DKA in adults aged 16 years and over within the first 4 hours of presentation (for paediatric management go to www.bsped.org.uk )

**Definition:** Severe uncontrolled diabetes with ketonaemia / ketonuria, metabolic acidosis, usually with hyperglycaemia.

**Severe DKA = pH < 7.1 or $HCO_3^-$ < 5 mmol/L or $H^+$ > 80 mEq/L**

*Ideally patients with DKA should be managed in a MHDU setting.*

Consultant / Senior physician should be called immediately if:

- Cerebral Oedema
- Severe DKA
- Hypokalaemia on admission
- Reduced conscious level

The new national protocol for the emergency management of DKA should be used for all eligible patients (for paediatric management go to www.bsped.org.uk) and is briefly outlined in this guideline. It is currently being rolled out on all acute sites (**N.B.** If your site has not adopted the new protocol yet, then follow your own in-house guideline until it is).

With the new national protocol please ensure care pathways for 0 - 4 hours and 4 hours - discharge are completed for each DKA episode. These provide instruction on appropriate fluid, insulin and potassium replacement. National audits have highlighted that the most common errors in managing DKA are delay in starting fluids and/or insulin and inadequate monitoring of potassium.

The care pathways for the new DKA protocol are available within relevant departments or online at:

**Care Pathway 0 - 4 hours –**

www.diabetesinscotland.org.uk/Publications/DKA%20Care%20Pathway%201%20v10.pdf

**Care Pathway 4 hours - discharge –**

www.diabetesinscotland.org.uk/Publications/DKA%20Care%20Pathway%202%20v12.pdf

**Additional supporting guidance for care pathway 4 hours - discharge see:**
StaffNet, Clinical Guideline electronic resource directory, search in endocrine section

**General: from 4 hours**

- Review blood glucose (BG) and U&Es
- Prescribe usual long-acting insulin at usual time.
- Check blood glucose, U&Es and bicarbonate 4 hourly.
- Continue 0.9% sodium chloride with KCl at 250 ml/hour until blood glucose < 14 mmol/L.

**Fluids and insulin: when blood glucose < 14 mmol/L**

- Start 10% glucose with 20 mmol KCl at 100 ml/hour (do not stop this unless advised by consultant or diabetes specialist).

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- 0.9% sodium chloride rate reduced to 150 ml/hour (with 10 mmol/L KCl if potassium 3.5 - 5 mmol/L, or 20 mmol/L KCl if potassium < 3.5 mmol/L)
- Reduce insulin infusion rate to 3 units/hour

**Insulin infusion rate: on hourly blood glucose check**

- If > 14 mmol/L, increase insulin rate by 1 unit/hour
- If < 9 mmol/L, decrease insulin rate by 1 unit/hour
- If < 3.5 mmol/L, stop insulin for an hour, restart at 1 unit/hour if > 3.5mmol/L
- If persistently above 14 mmol/L, despite increasing insulin to 6 units/hour, ask for medical review and check pump devices, IV lines and IV cannulae to ensure patient is getting prescribed insulin dose.

**Consider introducing SC insulin (and stopping IV insulin)**

- When venous bicarbonate normal, and patient eating normally
- Stop IV fluids and IV insulin 30 minutes after injection of usual pre-meal SC insulin
- In cases where unsure what insulin to start or what dose to use contact diabetes specialist

## Key steps in the management of DKA

1. Ensure all paediatric / adolescent patients are managed using a paediatric protocol.
2. Confirm the diagnosis ($H^+$ > 45 mEq/L or $HCO_3^-$ < 18 mmol/L or pH < 7.3 on venous gas with ketonaemia or ketonuria).
3. Initiation of IV fluids within 30 minutes of arrival.
4. Initiation of IV insulin within 1 hour of arrival.
5. Regular monitoring of $K^+$ level and appropriate replacement.
6. Commence IV glucose infusion once BG < 14 mmol/L.
7. Convert back to usual mealtime SC insulin regimen when $HCO_3^-$ within normal reference range and patient is eating normally (stop IV fluids and IV insulin 30 minutes after usual injection of pre-meal SC insulin).

## Supplementary notes as per Care Pathway 0 - 4 hours

1. **Guidance on bicarbonate**: Do not use bicarbonate.
2. **Potassium replacement**: administer at rate < 20 mmol/hour of KCl.
3. **WBC count**: This is often raised in DKA. Only give antibiotics if there is clear evidence of infection.
4. **Blood glucose >14 mmol/L**: If this rises > 14 mmol/L do not stop glucose, adjust insulin to maintain level between 9 and 14 mmol/L. See guidance above regarding insulin dose adjustment. *Do not stop glucose once started*.

*Continues on next page*

5. **Signs of cerebral oedema**: Children and adolescents are at the highest risk. Consider if: headaches, or reduced conscious level. Monitoring for signs of cerebral oedema should start from the time of admission and should continue until up to at least 12 hours after admission. If there is a suspicion of cerebral oedema or the patient is not improving as expected, within 4 hours of admission, call the consultant. Consider ITU (check arterial blood gases). Administer:

   **Mannitol IV (100 ml of 20% over 20 minutes) or dexamethasone IV 8 mg (discuss with Consultant)** and undertake CT scan to confirm findings.

6. **Laboratory blood glucose testing**: It is reasonable to use a point-of-care blood glucose meter to monitor BG level if the previous laboratory BG value is < 20 mmol/L.

7. **Insulin managemen**t: Insulin should be prescribed, beginning at 6 units/hour. Rate will generally be reduced with time depending on clinical circumstances, presence of long-acting insulin and to avoid a fall of > 5 mmol/L per hour as rapid falls in blood glucose may be associated with cerebral oedema.

8. **Assessment of response to insulin**: Sensitivity to insulin can vary markedly with time and between patients. If BG level is not falling, always check pump devices, IV lines and IV cannulae to ensure patients are getting prescribed insulin dose. Consider other causes that could be contributing: sepsis, steroid therapy, obesity or liver disease.

## Supplementary notes as per Care Pathway 4 hours – discharge

1. **Consider precipitating factors**: Common causes include:

   Omissions of insulin, infection, newly diagnosed diabetes, myocardial infarction or a combination of these factors.

   Some or all of the following may have contributed to the DKA episode:

   Errors in insulin administration, faulty equipment, practical problems.

2. **Refer for specialist diabetes review**: Whenever possible, all patients should be notified to the diabetes team within 12 hours of admission.

*Ensure insulin is prescribed before patient leaves hospital. This must include the specific type of insulin, dose and appropriate device.*

# Management of Hyperglycaemic Hyperosmolar State / Hyperosmolar Non-Ketotic Coma (HONC)

This condition carries a significant mortality and close monitoring within a well staffed clinical area is essential. The following regimen is a guide only; because of the co-morbidities associated with this condition each case must be treated on an individual basis.

## Introduction

Diagnostic criteria include:

- Severe hyperglycaemia (blood glucose > 30 mmol/L)
- Total osmolality > 340 mosmol/kg
- Serum bicarbonate > 15 mmol/L (not acidotic)
- Urinary ketones ≤ + plus

Clinical features include:

- Insidious onset
- Severe dehydration
- Impaired level of consciousness (degree correlates with plasma osmolality).
- May have concurrent illness e.g. MI, stroke or pneumonia.

This condition occurs in patients with type 2 diabetes mellitus (which may or may not have been previously diagnosed). There is marked hyperglycaemia and dehydration without significant ketosis and acidosis. The condition usually develops over a period of days, often made worse by diuretics and consumption of glucose rich drinks.

The aim should be for a **gradual** restoration of blood biochemistry avoiding a rapid reduction in plasma osmolality (which can precipitate cerebral oedema). These patients commonly have co-existing medical problems and mortality is much higher than for DKA. There is also a significant risk of thromboembolism and thromboprophylaxis should always be used in the absence of contraindication.

## Key steps in the management of HHS / HONC

- Establish correct diagnosis
- Monitor closely in a well staffed clinical area
- Aim to reduce blood glucose gradually
- Appropriate fluid resuscitation must be guided by clinical assessment, hydration status and co-morbidity.
- Regular monitoring of potassium level must guide appropriate replacement
- Consider and treat the underlying cause.

*Continues on next page*

## Assessment / monitoring

- Glucose – often exceeds 40 mmol/L
- U&Es – patient is dehydrated and can be hypernatraemic
- Venous blood gases – are relatively normal (not acidotic as seen in diabetic ketoacidosis (DKA))
- Osmolality – is calculated by [2 x ($Na^+$ + $K^+$) + urea + glucose]. It is usually > 350 mosmol/kg
- FBC – increase in Hb and WCC may indicate dehydration and infection
- ECG – may show ischaemia or infarction
- Chest x-ray
- Urinalysis
- MSSU / blood cultures

## General management and drug therapy

IV insulin and IV fluid replacement are the mainstays of treatment but both should be used more cautiously compared to DKA (see below).

- Give oxygen therapy.
- Central venous pressure (CVP) monitoring may be required to guide fluid replacement.
- Insert nasogastric tube if consciousness level is reduced or protracted vomiting.
- Insert urinary catheter.
- Give thromboprophylaxis SC, if no contraindications.

  **Enoxaparin SC 40 mg once daily (or 20 mg once daily if the eGFR is < 30 ml/minute/1.73m$^2$).**

### IV Fluids

Administer: **Sodium chloride IV 0.9%:** **Give 1st litre over 1 hour,**
**2nd litre over 2 hours**
**3rd litre over 4 hours**
**4th litre over 6 hours and**
**5th litre over 8 hours**

- Faster rehydration is inappropriate in hyperosmolar coma. The above regimen is a guide and should be reviewed in the elderly or patients with cardiac disease according to clinical assessment of hydration and taking into account co-morbidities.
- If the corrected sodium concentration is high (> 155 mmol/L) after the initial 1 - 2 litres of sodium chloride, then 0.45% sodium chloride should be considered after discussion with the consultant on-call or diabetes team. Serum electrolytes should be monitored closely.
- When blood glucose (BG) level falls below 14 mmol/L add in 10% glucose at a rate of 100 ml/hour.
- Review the patient closely to determine hydration status and consider the need for, and rate of rehydration with sodium chloride 0.9% solution.

**Continues on next page**

**General management and drug therapy continued from previous page**

### IV Insulin (soluble insulin e.g. Actrapid® or Humulin S®)

Preparation: Add 50 units of soluble insulin (Actrapid® or Humulin S®), drawn up using an insulin syringe, to 50 ml of 0.9% sodium chloride in a 50 ml syringe (1 unit/ml infusion). Infuse intravenously using a syringe pump.

A starting infusion rate similar to the one used in DKA can be used. Start at 6 units/hour of insulin. Aim for a target blood glucose of between 9 and 14 mmol/L. The additional supporting guidance from Diabetes Ketoacidosis care pathway 4 hours - discharge on page 276 can be used to adjust insulin dose when blood glucose has fallen to < 14 mmol/L.

**Remember:**

- Aim for a gradual reduction in blood sugar in order to prevent sudden osmotic shifts.
- Aim for a fall in BG at a rate of 2 - 3 mmol/hour. It may be necessary to adjust the infusion rate to achieve this. If the fall in BG is too rapid with 6 units/hour of insulin then consider reducing the rate to 3 units/hour.
- When BG falls below 14 mmol/L add in 10% glucose 100 ml/hour.
- Be prepared to adjust insulin infusion rate to maintain BG within the target range.
- If BG level is not falling, **always** check pump devices, IV lines and IV cannulae to ensure patients are getting prescribed insulin dose. Consider other causes that could be contributing: sepsis, steroid therapy, obesity or liver disease.

### Potassium monitoring and replacement

- The initial serum potassium can be normal or elevated but the potassium level may fall in response to the patient being treated with insulin. It is therefore essential that Urea and electrolytes are checked on admission, and at 2 hours and at 4 hours into admission to guide appropriate potassium replacement.
- Aim for a serum potassium of 4 – 5 mmol/L. IV fluids containing potassium (unless patient anuric) can be used to maintain potassium within this range.

| **Serum Potassium (mmol/L)** | **Potassium chloride to be given (mmol/L)** (**N.B.** Potassium bags are available as 20 mmol/500ml) |
|---|---|
| > 5 | 0 |
| 3.5 - 5 | 20# |
| < 3.5 | 40 |

# To give potassium chloride 20 mmol/L give one 500 ml bag of fluid containing potassium chloride 20 mmol and then run through a bag of 500 ml fluid not containing any potassium.

- The usual maximum rate of potassium administration is 10 mmol/hour. Faster rates can be given but ensure ECG monitoring is done.

**N.B.** Do not administer potassium chloride at a rate > 20 mmol/hour under any circumstances.

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**Important points**

1. This regimen is a guide and should be modified according to response to therapy.
2. Urea and electrolytes should be checked at least four times daily to guide potassium administration but may need to be more frequent depending on clinical scenario.
3. Continue IV fluids and insulin until normal biochemistry is restored and patient is eating and drinking normally. This may take up to 48 – 72 hours.
4. Recommence insulin or oral hypoglycaemics in patients previously treated. Many patients who were previously undiagnosed can be managed on diet therapy alone. Some will require oral hypoglycaemics (see page 291 for information on types of drugs).
5. Discuss with a member of the Diabetes Team pre-discharge.

*If you are unsure of how to review or how to adjust any of these parameters please contact a member of your local Diabetes Team.*

# Management of Diabetes for People Receiving Enteral Feeding in Hospital

## Introduction

When patients with diabetes mellitus are being artificially fed via the enteral route (e.g. nasogastric, gastrostomy or jejunostomy) *glycaemic control can prove difficult*. This may complicate their medical condition and delay recovery. To maintain optimal glycaemic control while ill and receiving enteral nutrition, patients may require alteration of their usual diabetes treatment. It is imperative that there is good communication between the Diabetes Team, the Nutrition Support Dietitian, and the extended medical teams.

**This guideline is aimed at patients who:**

1. Are currently on 24 hour feeding and IV insulin being transferred to SC insulin.
2. Have pre-existing diabetes and require enteral feeding.
3. Develop hyperglycaemia while being enterally fed.

## Target glycaemic control

For patients being enterally fed, the extremes of glycaemic control should be avoided. A target blood glucose reading should be between 6 and 12 mmol/L. These targets should be adjusted according to individual patient requirements.

### Diabetes therapy

The majority of patients with diabetes will experience a rise in their blood glucose levels when they commence enteral nutrition. There are often other factors such as infection and recent surgery that will affect glycaemic control. The following principles should be adhered to:

- Oral hypoglycaemic agents may not provide adequate glycaemic control. In this instance the patient should usually be converted to insulin and the oral hypoglycaemic agent should be discontinued.
- The usual therapy of choice is insulin, initially via an IV sliding scale, see Table 1 on next page.
- Frequently re-evaluate the sliding scale regimens as the insulin dose may need to be adjusted to achieve target glycaemic control.
- Once the patient's blood glucose is stabilised and feeding has been established, he / she should be converted to SC insulin injections.
- Discontinue the IV infusion once the initial SC injection has been administered.
- SC insulin dose can be calculated as follows:
  1. Take an average of the patients 24 hour insulin requirements on the intravenous sliding scale.
  2. Subtract 25% from this value and this will be their ***total daily insulin dose***.
  3. This will usually be split into 2 or more injections (see section on feeding regimens).

*Continues on next page*

- Retrospective treatment with corrective doses of SC insulin should be avoided, instead the insulin doses should be increased prospectively i.e. ***avoid boluses of short-acting insulin***.

**Table 1 – Insulin IV sliding scale regimen**

**Add 50 units of soluble insulin (Actrapid® or Humulin S®) to 50 ml of 0.9% sodium chloride in a 50 ml syringe. Infuse IV using a pump and adjust according to sliding scale:**

| Blood Glucose (mmol/L) | Infusion Rate ( units/hour) |
|---|---|
| < 5 | 0 |
| 5.1 - 10 | 1 |
| 10.1 - 15 | 2 |
| 15.1 - 20 | 3 |
| > 20.1 | 4 **and call a doctor** |

Check capillary blood glucose hourly initially then 2 hourly.

**N.B.** *If blood glucose regularly outwith range of 6 – 12 mmol/L, insulin doses should be reassessed.*

## Maintaining glycaemic control

- If the feed stops unexpectedly, blood glucose levels should be closely monitored, as patients are at risk of hypoglycaemia. If necessary, an IV glucose infusion should be commenced until feeding can be resumed.
- If feed is stopped electively the patient may require to recommence IV insulin and glucose, depending on length of fast.

# Enteral feeding regimens

For inpatients with diabetes, the enteral feeding regimen will be recommended by the dietitian to meet the individual's nutritional requirements. To maximise glycaemic control, we suggest using the following feeding regimens:

**Intermittent feeding –**

1. **May be commenced at varying times and be of variable duration (minimum 12 hours, maximum 20 hours).**
2. **Calculate total daily insulin SC dose – average 24 hour IV requirements minus 25%.**
3. **Administer 2/3 of the dose as pre-mixed 30 / 70 insulin SC ( Humulin M3®) at the start of the feed. Discontinue IV insulin after the first SC dose has been administered.**
4. **Administer the remaining 1/3 of the insulin SC dose as isophane (either Insulatard® or Humulin I®) at 12 hours.**

*Continues on next page*

**Bolus feeding –**

1. **The feed is divided into at least 4 boluses, ensuring the carbohydrate intake is evenly distributed throughout the day, to mimic breakfast, lunch, dinner, supper and between meal snacks.**
2. **Calculate total daily insulin SC dose as above. (i.e. average 24 hour IV requirements minus 25%).**
3. **Administer 2/3 of the dose as pre-mixed 30 / 70 insulin SC (Humulin M3®) before the breakfast bolus feed. Discontinue IV insulin after the first subcutaneous dose has been administered.**
4. **Administer the remaining 1/3 of the dose as pre-mixed 30 / 70 insulin SC (Humulin M3®) around 9 - 10 hours later but before the dinner bolus feed.**

Glycaemic control should be closely monitored and insulin doses should be adjusted accordingly, if advice on insulin adjustment is required, contact the Diabetes Team.

## Key points

- *Hypoglycaemia is a medical emergency and should be treated urgently*. If the patient is on IV insulin, stop the pump immediately. To treat hypoglycaemia give:

  **20 g quick-acting carbohydrate via enteral tube: e.g. 50 - 70 ml of Ensure Plus® Juce or 100 mls of original Lucozade®, then flush.** Check blood glucose after 10 - 15 minutes. Repeat treatment up to three times until glucose > 4 mmol/L. Refer to full hypoglycaemia guideline on page 288.

  You must always follow up with another feed bolus or by recommencing the feed to prevent the blood glucose falling again. If the tube has been dislodged or the patient is unconscious you will need to gain IV access and administer bolus IV glucose (see page 289).
- For patients receiving enteral nutrition, extremes of glycaemia should be avoided and target blood glucose levels should be between 6 and 12 mmol/L. All patients with type 1 diabetes must have their urine checked for ketones daily.
- Patients with diabetes who are commenced on enteral feed will usually require an increase in their diabetes medication or conversion into insulin.
- If a patient on enteral nutrition becomes hyperglycaemic, then the diabetes therapy needs adjusting, rather than a reduction in nutrition. This usually requires an increase in the insulin dose.
- Communication between the Diabetes Team and all of the healthcare professionals looking after the patient is vital, and the targets for blood glucose control should be established for the individual patient, avoiding hypoglycaemia.
- As the patient's clinical condition improves and activity level increases, insulin requirements may reduce significantly. If the patient comes off enteral feeding and returns to normal eating, they should usually return to their pre-illness diabetes regimen.

# Insulin Sliding Scale (Not for use in DKA, HHS / HONC patients)

This sliding scale should NOT to be used to treat people with Diabetic Ketoacidosis (DKA) or Hyperglycaemic Hyperosmolar State (HHS) / Hyperosmolar Non-Ketotic Coma (HONC). See individual guidelines on page 276 and 279.

This sliding scale can be used to manage glucose levels in people with diabetes mellitus. It can be used in surgical patients with diabetes mellitus undergoing operations however local anaesthetic departments may have their own scales. *Prior to using the scale below, discuss with local anaesthetists that they are happy for it to be used.* This scale can also be used in medical patients with diabetes mellitus in whom regulation of glucose is deemed important. The principles of the sliding scale are:

- Desired glucose control is achieved and maintained
- Avoidance of hypoglycaemia
- Avoidance of ketosis by providing adequate carbohydrate and insulin
- Maintenance of fluid and electrolyte balance.

Before starting on the sliding scale it is important to specify the target glucose level and whether intravenous fluids are to be given with insulin. Urea and electrolytes should be checked before starting the sliding scale to guide potassium administration.

## Insulin

Preparation: **Add 50 units of soluble insulin (Actrapid® or Humulin S®), drawn up using an insulin syringe, to 50 ml of 0.9% sodium chloride in a 50 ml syringe.** Infuse IV using a syringe pump and adjust according to sliding scale below, which is an initial guide. Please review insulin rate and blood glucose response on a regular basis (see supplementary notes on next page) and amend if need be to achieve target blood glucose.

**Table 1 – Insulin sliding scale (initial guide)**

| Blood glucose (mmol/L) | Insulin Infusion Rate (units/hour) |
|---|---|
| < 5 | 0 |
| 5.1 - 10 | 1 |
| 10.1 - 15 | 2 |
| 15.1 - 20 | 3 |
| >20.1 | #4 and call a doctor (see below) |

# See also supplementary notes on next page

### Intravenous Fluids (if being given)

The fluid regimen used with this sliding scale is NOT appropriate for fluid resuscitation. If intravenous fluids are to be given consider using the following regimen (see notes on next page) regarding potassium supplementation).

1. 500 ml bag of 5% glucose containing 20 mmol KCl (potassium chloride) over 5 hours THEN
2. 500 ml bag of 5% glucose containing 20 mmol KCl over 5 hours THEN
3. 500 ml bag of 5% glucose containing 20 mmol KCl over 5 hours THEN
4. 500 ml bag of 5% glucose / 0.9% sodium chloride over 5 hours THEN repeat the process, beginning at number 1.

*Continues on next page*

## Potassium Supplementation

Aim for a serum potassium of 4 - 5 mmol/L.

Be guided on potassium replacement by U&Es:

- If baseline potassium is > 5 mmol/L omit potassium replacement but continue to monitor potassium and re-check U&Es in 4 hours.
- Be prepared to vary the potassium chloride content of the IV fluids according to plasma potassium levels.
- In patients with renal failure, chronic kidney disease or oliguria seek advice from a member of the Renal or Diabetes Team or Senior Medical Staff on potassium replacement.

## Supplementary Notes

- Check capillary blood glucose hourly except when it is < 5 mmol/L and the sliding scale is stopped. In this instance check the capillary blood glucose every 30 minutes. When blood glucose levels are stable capillary blood glucose levels can be checked every two hours.
- When blood glucose levels are > 20.1 mmol/L it is important to assess the following:
  - Check pump devices, IV lines and IV cannulae to ensure patients are getting the prescribed insulin dose
  - Consider other causes that could be contributing: sepsis, steroid therapy, obesity.

Review the following at least twice daily (may need to be more frequent depending on the clinical scenario):

- Sliding scale and blood glucose response
- Rate of infusion and type of fluid used
- Potassium level and potassium supplementation.

*If you are unsure of how to review or how to adjust any of these parameters please contact a member of your local Diabetes Team. In patients with type 1 diabetes the sliding scale should only be discontinued once SC insulin (containing a long-acting insulin, such as a premixed or background insulin) has been restarted.*

# Management of Hypoglycaemia

## Introduction

Hypoglycaemia is a serious condition and should be treated as an emergency regardless of the patient's level of consciousness. All documented blood glucose values < 4 mmol/L can be considered a hypoglycaemic event and should not be tolerated in any patient on a regular basis. The signs and symptoms of hypoglycaemia can be variable and a high index of suspicion is often required. Some patients experience hypoglycaemic symptoms where the blood glucose level is not < 4 mmol/L. If this happens a small carbohydrate snack can be given for symptom relief.

**Table 1 – Symptoms of hypoglycaemia**

| Autonomic | Neuroglycopaenic |
|---|---|
| Trembling | Difficulty concentrating |
| Sweating | Confusion |
| Anxiety | Weakness |
| Hunger | Drowsiness |
| Palpitations | Visual change |
| Nausea | Difficulty speaking |
| Tingling | Headache |
| | Dizziness |
| | Tiredness |

By far the commonest cause of hypoglycaemia is treatment with insulin or sulphonylurea drugs in patients known to have diabetes. This may be accidental or deliberate. Patients taking sulphonylurea drugs who have a hypoglycaemic episode should be admitted for at least 24 hours for monitoring.

## Assessment / monitoring

- Send blood glucose to the lab for a level. Glucostix® can be inaccurate at low blood glucose concentrations. Waiting for the result should not delay giving appropriate treatment.
- Assess whether hypoglycaemic episode is:
  **Mild** – autonomic symptoms may be a feature (see table above).
  **Moderate / severe** – autonomic and neuroglycopaenic symptoms may be a feature. Plasma glucose is typically < 2.8 mmol/L and can result in coma if left untreated.
- Once patient is stabilised (see general management and drug therapy section on the next page on how to do this), investigate:
  - Likely cause of the episode (missed meal, dosage error, increased exercise, alcohol excess, deliberate overdose).
  - Establish the presence of hypoglycaemic 'warning symptoms' i.e. sweating, tremor, and tachycardia. These may be impaired in patients with longstanding diabetes.

*Continues on next page*

# General management and drug therapy

For further information see the full guideline "The Hospital Management of Hypoglycaemia in Adults with Diabetes Mellitus" at www.diabetesinscotland.org.uk/publications.aspx

**Mild Hypoglycaemia** – Patient is conscious, orientated and able to swallow. Treat with **15 - 20 g of quick-acting carbohydrate** such as:

**Dextrosol® 5 - 7 tablets or Glucotabs® 4 - 5 or**

**Original Lucozade® 90 - 120 ml or**

**Pure fruit juice* 150 - 200 ml**

Test blood glucose level after 15 minutes, and if still < 4 mmol/L, repeat above treatment options up to 3 times. If still hypoglycaemic call a doctor and consider **glucose IV (as per severe hypoglycaemia section below) or Glucagon** IM 1 mg (only give once).**

Blood glucose level should now be > 4 mmol/L. Give **20 g of long-acting carbohydrate e.g. two biscuits / slice of bread / milk 200 - 300 ml / next meal containing carbohydrate (give 40 g of long-acting carbohydrate if IM Glucagon has been used).**

**Moderate Hypoglycaemia** – Patient is conscious and able to swallow, but confused, disorientated or aggressive. If capable and cooperative treat as for mild hypoglycaemia above. If not capable and cooperative but can swallow give 1.5 - 2 tubes of GlucoGel® (squeezed into mouth between teeth and gums). If ineffective use Glucagon** IM 1 mg (only give once).

Test blood glucose level after 15 minutes, and if still < 4 mmol/L, repeat steps above up to 3 times. If still hypoglycaemic call a doctor and consider **IV glucose (as per severe hypoglycaemic section**).

Blood glucose level should now be above 4mmol/L. **Give 20 g of long-acting carbohydrate e.g. two biscuits / slice of bread / milk 200 - 300 ml / next meal containing carbohydrate (give 40 g of long-acting carbohydrate if IM Glucagon has been used)**.

**Severe Hypoglycaemia** – Patient is unconscious / fitting or very aggressive or nil-by-mouth (NBM). Check ABC, stop insulin (if on IV) and contact doctor urgently. Give:

**Glucose IV over 10 minutes as:** **20% glucose 75 ml *or***
**10% glucose 150 ml *or***
**50% glucose 30 ml *or***
**Glucagon** IM 1 mg** (only give once)

**N.B.** There is risk of extravasation injury with glucose 50%, only use if 10% or 20% not available.

Re-check glucose after 10 minutes and if blood glucose still < 4mmol/L repeat IV glucose above. If glucose now > 4mmol/L and conscious and swallow safe give **20 g of long-acting carbohydrate e.g. two biscuits / slice of bread / milk 200 - 300 ml / next meal containing carbohydrate (give 40 g of long-acting carbohydrate if IM Glucagon has been used). If NBM, once glucose > 4 mmol/L give glucose 10% infusion at a rate of 100ml/hour* until no longer NBM or reviewed by doctor.**

* In patients with renal / cardiac disease use intravenous fluids with caution. Avoid fruit juice in renal failure.

*Continues on next page*

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**Glucagon may take up to 15 minutes to work and may be ineffective in undernourished patients, in severe liver disease and in repeated hypoglycaemia. Do not use in oral hypoglycaemia agent induced hypoglycaemia. Patients may experience abdominal discomfort and vomiting after glucagon administration.

## Supplementary notes

- The volumes of IV glucose suggested are less than the total volume of the bag therefore care should be taken not to over-infuse. The method of administration should be governed by the clinical urgency.
- 50% glucose is irritant to blood vessels and should only be used when alternative solutions are not readily available. 10% AND 20% glucose are less likely to be irritant to veins.
- After a severe hypoglycaemic episode patients will often have a high glucose for several hours due to the counter regulatory hormonal response and as a result of the exogenous glucose administration.
- Long-acting insulins and oral hypoglycaemic drugs e.g. gliclazide, may be associated with prolonged hypoglycaemia requiring IV glucose infusion (for 24 hours or more) and regular (at least hourly) blood glucose monitoring.
- Once patient is stabilised each episode of hypoglycaemia should be investigated:
  - Likely cause of the episode (missed meal, dosage error, increased exercise, alcohol excess, deliberate overdose).
  - Establish the presence of hypoglycaemic 'warning symptoms' i.e. sweating, tremor, and tachycardia. These may be impaired in patients with longstanding diabetes.

## Other information

Review educational and emotional support needs before discharge (liaise with the diabetes team). All patients with diabetes and their relatives and carers should receive information about diabetic emergencies. Key points to address include:

- The potential consequences of diabetic emergencies
- How diabetic emergencies can be prevented
- Be able to identify the early signs of diabetic emergencies and know what action they should take
- Know what action to take during intercurrent illness i.e. 'sick day rules'

# Types of Antidiabetic Drugs

## Injectable therapies

### Insulins

For all patients starting insulin for the first time please contact a diabetic nurse specialist (most patients are started on twice daily mixed insulin). When prescribing insulin please specify the type and dose on both the drug kardex and insulin prescription chart.

Short-acting insulin

- Humalog® (insulin lispro)
- NovoRapid® (insulin aspart)
- Humulin S®
- Actrapid®

Intermediate- and Long-acting insulin (basal)

- Humulin I®
- Insulatard®
- Insulin glargine (Lantus®)
- Insulin detemir (Levemir®)

Mixture of short- and intermediate-acting: Mixed insulin

- Humulin M3®
- Humalog® Mix25
- Humalog® Mix50
- Novomix® 30

The list above reflects the majority of types of insulin used locally. For a complete reference of all insulins, refer to BNF.

**N.B. Do not** give hyperglycaemic patients boluses of SC insulin on an 'as required' basis, adjust their regular therapy instead. Check urine for ketones. If ketones found then follow local guidelines, which may necessitate starting an insulin sliding scale.

## Insulin prescribing – Important points

Insulin is an important medication that when prescribed poorly can lead to severe complications and even mortality. Below are four key components to safer insulin prescribing (full guidance is available on StaffNet, Clinical Guideline Electronic Resource Directory, and search in "Endocrine system"):

1. The right insulin – *ensure that the correct insulin is prescribed in full in both the Kardex and the insulin prescription chart*. Check with the patient and the GP if necessary.

**Note:** Remember – the "25" in Humalog Mix 25 and the "30" in Novomix 30 refers to the percentage of rapid acting insulin in the mix, not the dose.

2. The right time – prescribe insulin at the right time to reduce risk of hypoglycaemia

   **Example:** Short-acting insulin should be prescribed before meals (can be written before breakfast, before lunch, before dinner).

   Premixed twice daily insulin such as Novomix 30 is generally prescribed before breakfast and evening meal.

   If possible, prescribe evening dose of long-acting insulin earlier in the day and morning dose of insulin the day before. Use the previous day's results to guide you. If you cannot prescribe next morning insulin dose, tell the night shift to ensure insulin is given with breakfast where appropriate.

*Continues on next page*

3. The right dose – confirm insulin dose with two sources as per Medicines Reconciliation Policy (see page 3). *Do not use abbreviations such as IU or U – write "units" in full where indicated*.
4. The right way – only use an insulin syringe to draw up insulin. **Never use a normal syringe**.

**Glucagon-like peptide 1 (GLP-1) agonists** – *only initiate on specialist advice.* This class includes:

- Exenatide (Byetta®)
- Liraglutide (Victoza®)
- Exenatide LAR (Bydureon®)

See BNF for dosing details and contraindications. See GGC Formulary for restrictions on use.

## Oral antidiabetic drugs

### Biguanides

- **Metformin 500 mg once daily for 1 week with evening meal, then 500 mg twice daily for at least 1 week, then 500 mg three times daily for at least 1 week, then 1000 mg twice daily.**

  **N.B**. Avoid metformin if eGFR is < 45 ml/minute/1.73m$^2$.

Patients can experience some gastrointestinal upset with metformin. By starting at a low dose with food this is less likely. Normally these symptoms will resolve so it is worthwhile advising patients to persevere with it. Contact the diabetes team if in doubt and if further advice is needed.

### Sulphonylureas

- **Gliclazide: initially 40 - 80 mg daily, at mealtime, adjusted according to response. Maximum 320 mg daily.** Alternative to gliclazide is glipizide (see BNF for details).

**Glitazones** – *only initiate on specialist advice*.

- **Pioglitazone initially 15 - 30 mg daily once increased to 45 mg daily according to response.**

Follow BNF instructions regarding monitoring LFTs after initiation of therapy.

**Dipeptidyl peptidase IV inhibitors** – *only initiate on specialist advice*. This class includes:

- Sitagliptin
- Vildagliptin
- Saxagliptin
- Linagliptin

**Sodium-glucose co-transporter 2 inhibitor** – *only initiate on specialist advice.*

- Dapagliflozin

See BNF for dosing details and contraindications. See GGC Formulary for restrictions on use.

Contact the diabetes team if in doubt when prescribing oral antidiabetic drugs and if further advice is needed.

# Management of Adrenal Insufficiency

## Introduction

The adrenal cortex is responsible for producing glucocorticoids, mineralocorticoids and androgens. When there is insufficiency it can either be primary related (e.g. there is structural damage to the gland) or secondary related (e.g. suppression of hypothalamic-pituitary axis by various factors).

This guideline advises on the general management of adrenal insufficiency in an acute situation and the diagnosis of it in the non-acute.

## Assessment / monitoring

**If patient has suspected acute adrenal insufficiency:**

- Establish venous access and draw blood for electrolytes, glucose, cortisol and ACTH. Then see General management and drug therapy section below.

**To diagnose adrenal insufficiency:**

- In stable patients in whom hypothalamic-pituitary-adrenal failure is suspected, perform a short Synacthen® (Tetracosactide acetate, ACTH) test:
  - Synacthen® 250 micrograms IM or IV
  - Sample cortisol at baseline and 30 minutes after Synacthen®. If unsure how to interpret results, seek specialist endocrine advice.

Then see General management and drug therapy section below.

## General management and drug therapy

### Acute adrenal insufficiency

- **Give hydrocortisone IV 100 mg immediately then every six hours.**
- **Fluid resuscitate with 0.9% sodium chloride.** Continue IV fluids for the next 24 - 48 hours, depending on the severity of illness and co-morbidity.
- If hypoglycaemic (blood glucose value < 4 mmol/L) give
  **125 ml of 20% glucose or 250 ml of 10% glucose IV.**
- Once patient is stable and eating / drinking convert patient over to an oral glucocorticoid. If the precipitating illness is resolving, then reduce the maintenance dose over 72 hours e.g.
  **Convert IV hydrocortisone dose to oral 50 mg twice daily then over 72 hours reduce to 15 - 20 mg orally at 8 am and 5 - 10 mg orally at 5 pm.**

### Adrenal insufficiency – non acute situation

- Contact the Endocrine Team to arrange education, a Medic information bracelet and an emergency information card.
- Additional fludrocortisone is likely to be required in primary hypoadrenalism.

*Continues on next page*

# Other Information

## General advice on long-term use of corticosteroids

To prevent acute insufficiency in a patient on long-term steroids with an intercurrent illness, e.g. infection then:

1. Double the steroid dose.
2. If unwell / unable to take oral therapy, change to **hydrocortisone IV 100 mg three to four times daily.**
3. Patients on maintenance corticosteroids must be given steroid cover across any surgical procedure. See BNF for details.
4. Surgical procedures involving a general anaesthetic – consult with the anaesthetist.
5. Seek advice on adjustment of corticosteroid doses for patients with acute or severe intercurrent illness.

## Corticosteroid dose equivalences

Prednisolone 5 mg is approximately equivalent to:

- Hydrocortisone 20 mg
- Dexamethasone 750 micrograms
- Methylprednisolone 4 mg

**N.B.** An equivalent dose is not always appropriate. When converting between different corticosteroids consider whether a dose increase (e.g. to cover intercurrent illness, as above) or a dose decrease (when tapering dose down) is appropriate.

Section 9

# Electrolyte Disturbances

# Management of Hyperkalaemia (plasma $K^+$ > 5.5 mmol/L)

This guideline is under review. See online version on StaffNet or www.ggcprescribing.scot.nhs.uk for the most up to date information.

## Assessment / monitoring

- Plasma potassium
- ECG monitoring

## General management

- **Exclude spurious hyperkalaemia (venous blood gas sample in emergency or seek advice from Biochemistry) and check for ECG changes**.
- Identify and treat underlying cause where possible:
  - Potassium supplements, ACE inhibitors, potassium-sparing diuretics and spironolactone should be discontinued.
  - Renal failure – consider referral to renal unit.
  - Hypovolaemia – consider volume expansion with IV sodium chloride 0.9%.
  - Severe acidosis (often associated with renal failure).
  - Hypoaldosteronism, e.g. Addison's disease.
- If hyperkalaemia remains unexplained, more specialised investigation may be appropriate. Advice may be obtained from your local Biochemistry Department.

## Drug therapy / treatment options

1. **Confirmed plasma $K^+$ 5.5 - 6.5 mmol/L**

   **Calcium Resonium® oral 15 g three times daily (in water not fruit juice).**

   - Calcium Resonium will not lower potassium acutely. It is only licensed for hyperkalaemia due to anuria or oliguria.
   - Resonium A can be used if there is a risk of hypercalcaemia.
   - Monitor plasma $K^+$ daily until $K^+$ < 5.5 mmol/L.

2. **Confirmed plasma $K^+$ > 6.5 mmol/L and/or ECG changes**
   (Although treatment should not be delayed, result should be confirmed):

   **10 ml calcium gluconate 10% - slow IV injection over 5 - 10 minutes** *given by a doctor*
   (to antagonise the effect of potassium on the heart).

   **10 units soluble insulin (Actrapid®) in 50 ml glucose 50% IV. This may be repeated once and/or followed by an infusion of the same mixture at 5 - 10 ml/hour.**

   ***and/or***

   **5 - 10 mg nebulised salbutamol**

   **N.B.** There is a risk of extravasation injury with glucose IV 50%.

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## Notes

- Calcium gluconate may be repeated after 5 minutes if ECG changes persist.
- Check plasma $K^+$ and glucose one hour after glucose / insulin infusion.
- Glucose / insulin infusions should be repeated until plasma $K^+ < 6.5$ mmol/L.
- Hyperosmolal glucose infusions should not be used in diabetic ketoacidosis.

# Management of Hypokalaemia (plasma $K^+$ < 3.5 mmol/L)

## Assessment / monitoring

- Plasma potassium

## General management

- Replace potassium losses
- Identify and treat underlying cause where possible:
  - Loop / thiazide diuretics – consider combination with a potassium-sparing diuretic
  - Vomiting and diarrhoea
  - Intracellular potassium shifts, e.g. post-operation, coronary ischaemia, critical illness
  - Re-feeding
  - Hypomagnesaemia

**N.B.** If hypokalaemia remains unexplained, more specialised investigations may be appropriate. Advice may be obtained from your local Biochemistry Department.

## Drug therapy / treatment options

### General notes

- Oral potassium chloride is the treatment of choice for most patients.

  Effervescent tablets (Sando-K®), which each contain 12 mmol of potassium and 8 mmol of chloride, are preferable as modified release tablets (Slow-K®) may cause gastrointestinal ulceration.
- The dosage and duration of treatment depends on existing potassium deficit and whether there is continuing potassium loss.
- Larger doses may be required especially in patients with digitoxicity or diabetic ketoacidosis. Advice is available from your local Biochemistry Department.
- *Potassium supplements should not be given in severe renal impairment or if plasma $K^+$ > 5.0 mmol/L.*
- **Caution** should be used in patients with renal insufficiency or when ACE inhibitors or potassium-sparing diuretics are being administered concomitantly.

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## Suggested starting doses (but see notes on previous page)

**Oral potassium supplementation**

1. For plasma $K^+$ 3.0 - 3.5 mmol/L (approximate potassium deficit 200 mmol):

   **Sando-K® 2 tablets 3 times daily**

   **Notes**

   - Monitor plasma $K^+$ twice weekly until stable.
   - Once plasma $K^+$ stable or if plasma $K^+$ > 4.5 mmol/L, reassess requirement for supplementation.

2. Plasma $K^+$ 2.5 - 2.9 mmol/L (approximate potassium deficit 200 - 400 mmol):

   **Sando-K® 3 tablets 3 times daily**

   **Note**

   - Monitor plasma $K^+$ daily until plasma $K^+$ > 2.9 mmol/L and then manage as above.

3. Plasma $K^+$ < 2.5 mmol/L or cardiac arrhythmia (approximate deficit > 400 mmol):

   ***Intravenous supplementation is usually required.***

**Intravenous potassium supplementation**

- Intravenous supplements are indicated if patients cannot eat, are unlikely to absorb oral potassium or have profound hypokalaemia.
- Where possible use pre-prepared infusion bags. These are available as:
  - **20 mmol KCl in 500 ml sodium chloride 0.9% or glucose 5%**
  - **40 mmol KCl in 500ml sodium chloride 0.9% or glucose 5%**
- ***The rate of infusion should not normally exceed 10 mmol/hour.***
- 10 ml ampoules of strong potassium chloride containing 20 mmol potassium per ampoule are only available in intensive care areas and should not be used in ward areas unless in exceptional circumstances and under close supervision. These must be ordered in the controlled drug requisition book.
- If concentrations other than those mentioned above are required, contact your clinical pharmacist or Medicines Information for advice (see Appendix 6 for details).

# Management of Hypomagnesaemia

**N.B.** Use of magnesium for other indications e.g. eclampsia is outside the scope of this guideline.

The reference range for serum magnesium is 0.7 - 1 mmol/L.

Serum concentrations should be used in conjunction with presenting signs and symptoms to diagnose hypomagnesaemia (see notes below).

## 1. Adults with normal renal function

**Magnesium levels should be monitored daily, and the dose adjusted as necessary.**

See flow diagram on next page.

## 2. Adults with renal impairment

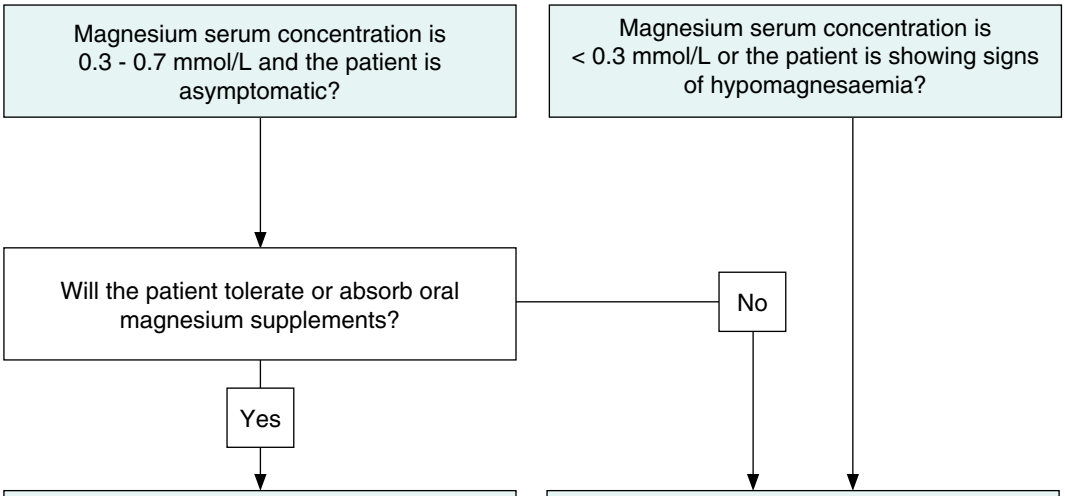
Patients with renal impairment should have the doses of magnesium halved as reduced urinary magnesium excretion puts the patient at risk of hypermagnesaemia.

### Additional information

- Magnesium is mainly an intracellular ion, so serum concentrations are not an exact measurement of total body stores.
- Magnesium depletion is often associated with other electrolyte abnormalities – reduced $K^+$, $Ca^{2+}$, $PO_4^{3-}$ or $Na^+$ levels may co-exist with a low $Mg^{2+}$.
- Possible symptoms include agitation, confusion, convulsions, weakness, tremors, ECG changes, nausea and vomiting.
- Establish and correct cause if possible.

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## Management of hypomagnesaemia in adults with normal renal function




**Oral magnesium supplements**
(unlicensed indication but widely used)

**Magnesium hydroxide mixture:**
**(5 ml contains 7 mmol magnesium)**
**up to 10 ml four times daily.**

***or***

**Magnesium oxide capsules 160 mg (named patient preparation):**
**(4 mmol magnesium per capsule)**
**1 or 2 capsules three times daily.**

***or***

**Magnesium glycerophosphate (named patient preparation):**
**(4 mmol magnesium per tablet)**
**3 - 6 tablets daily – may cause less diarrhoea.**

- Renal impairment – reduce dose by 50%.
- Monitor serum magnesium levels daily.
- Reduce dose if diarrhoea occurs.
- Magnesium glycerophosphate least likely to cause diarrhoea.

**Intravenous magnesium supplementation**

**as magnesium sulphate:**
**20 mmol to 30 mmol per day for up to five days.**

(Add 20 mmol (10 ml of magnesium sulphate 50%) to a 500 ml infusion bag of glucose 5% and infuse over 12 - 24 hours).

- Renal impairment – reduce dose by 50%.
- Monitor serum magnesium levels daily.

**N.B.** Doses shown are suggested starting doses. Further advice is available from your Biochemistry Department.

# Management of Hypophosphataemia

## Introduction

Hypophosphataemia may be asymptomatic, but clinical symptoms usually become apparent when plasma phosphate concentrations fall below 0.3 mmol/L. Possible symptoms include: weakness, anorexia, malaise, tremor, paraesthesia, seizures, acute respiratory failure, arrhythmias, altered mental status and hypotension,

## Assessment / monitoring

- Serum phosphate (reference range 0.7 - 1.4 mmol/L)
- Symptoms as above

## Drug therapy / treatment options

Suggested starting doses:

**Mild Hypophosphataemia (0.6 - 0.69 mmol/L):**

No treatment required.

**Moderate Hypophosphataemia (0.3 - 0.59 mmol/L):**

**Phosphate Sandoz® 1 - 2 tablets orally three times daily** (each tablet contains 16 mmol phosphate, 3 mmol potassium and 20 mmol sodium.)

Oral replacement is usually sufficient but consider intravenous replacement if patient has phosphate level 0.3 - 0.5 mmol/L and is symptomatic or nil by mouth or unlikely to absorb oral phosphate.

**Glycophos® IV 20 mmol (20 ml) in 500 ml glucose 5% over 12 hours**

Glycophos® solution (20 ml) contains 20 mmol phosphate (1 mmol/ml) and 40 mmol sodium (2 mmol/L.)

**Notes**:

- The dose should be reviewed daily according to phosphate levels.
- Diarrhoea is a common side effect of oral phosphate therapy and may necessitate a reduction in dose. Give in at least 120 ml of water to reduce risk of diarrhoea.

**Severe Hypophosphataemia (< 0.3 mmol/L)**

1. Phosphate level < 0.3 mmol/L and patient has impaired renal function:

   **Glycophos® IV 20 mmol (20 ml) in 500 ml glucose 5% over 12 hours.**

**Continues on next page**

**Drug therapy / treatment options continued**

2. Phosphate level < 0.3 mmol/L and patient has normal renal function:

   **Glycophos® IV 40 mmol given as 2 x 12 hour infusions,**

   ***i.e. 20 mmol (20 ml) in 500 ml glucose 5% over 12 hours x 2.***

   - Considering that the normal adult intake of phosphate is about 35 mmol per day, a reasonable typical IV replacement is 20 - 40 mmol per day.
   - For intravenous replacement Glycophos® has replaced Addiphos® as treatment of choice for hypophosphataemia as it contains no potassium and therefore removes associated risks.

   **Notes:**

   - Serum phosphate, potassium, calcium and magnesium levels should be monitored every 12 - 24 hours during IV phosphate administration.
   - Monitor renal function regularly.
   - Repeat the dose within 24 hours if an adequate level (> 0.64 mmol/L) has not been achieved.
   - Hypotension, hyperphosphataemia, hypocalcaemia, hypernatraemia, dehydration and metastatic calcification are possible adverse effects of intravenous phosphate therapy.

# Management of Hypercalcaemia

This guideline is under review. Please see the online version of the handbook for the most up to date guidance. In addition, for guidance on bisphosphonate use in cancer patients see www.intranet.woscan.scot.nhs.uk / Systemic anti-cancer therapy protocols / Supportive care

## Introduction

The reference range for adjusted serum calcium is 2.1 - 2.6 mmol/L.

**N.B.** In patients presenting with hypercalcaemia in an emergency setting always consider occult malignancy. Low serum albumin is another pointer to this being the cause.

## Assessment / monitoring

- Serum calcium should be monitored daily.
- U&Es to assess hydration status.

## Drug therapy / treatment options

If hypercalcaemia is life-threatening (adjusted calcium > 4 mmol/L), start:

**Sodium chloride 0.9% IV 1 litre over 4 hours and contact senior medical staff for advice immediately. Dialysis may be needed.**

Otherwise carefully rehydrate with:

**Sodium chloride 0.9% IV infusion 2 - 3 L over 24 hours to maintain urine output and promote calcium excretion.**

- More cautious rehydration will be necessary if the patient has a history of heart failure, renal failure or is elderly.
- Ensure thiazide diuretics are discontinued.
- After 24 - 48 hours of rehydration, consider intravenous pamidronate if the condition remains unresolved (see Table 1).

**Table 1 – IV Pamidronate dosing**

| Initial serum calcium (adjusted) mmol/L | Recommended total dose (mg) for tumour-induced hypercalcaemia |
|---|---|
| Up to 3 mmol/L | 15 - 30 |
| 3 - 3.5 mmol/L | 30 - 60 |
| 3.5 - 4 mmol/L | 60 - 90 |
| > 4 mmol/L | 90 |

**Continues on next page**

**Drug therapy / treatment options continued**

Give as a single infusion of pamidronate or in divided doses (infusions) over 2 - 4 consecutive days.

- The infusion rate should never exceed 20 mg/hour.
- The concentration of pamidronate in the infusion solution should not exceed 60 mg/250 ml.
- Pamidronate should not be used if CrCl < 30 ml/minute.
- Full effect of pamidronate may take 3 - 7 days.
- If corrected serum calcium continues to rise or has not returned to the reference range within 5 days zoledronic acid may be considered but its use is currently restricted within NHSGGC to “consultants treating tumour-induced hypercalcaemia and by specialist oncologists for the prevention of skeletal-related events in patients with breast cancer and multiple myeloma”.

# Management of Hypocalcaemia

## Introduction

The reference range for adjusted serum calcium is 2.1 - 2.6 mmol/L. Hypocalcaemia may be due to deficiencies of calcium homeostatic mechanisms, secondary to high phosphate levels or other causes.

## Assessment / monitoring

- Plasma calcium level
- Establish cause of hypocalcaemia and seek senior advice if necessary
- Assess whether patient is symptomatic (e.g. tetany)

## Drug therapy / treatment options

Recommended daily dose of elemental calcium is 1 - 3 g (2.25 - 6.75 mmol) daily.

### Oral

**Calcium salts – up to 50 mmol daily in 2 - 3 divided doses, for example:**

**Sandocal-1000 – 1 - 2 tablets (25 - 50 mmol) in water (other preparations are available)**

***If oral replacement is ineffective after 2 - 3 days in asymptomatic patients, add:***

**Alfacalcidol oral 1 microgram daily (elderly 500 nanograms).**

### Intravenous – for hypocalcaemic tetany

Initial:

**Calcium gluconate 10% 10 ml (2.2 mmol calcium) over at least 10 minutes with cardiac monitoring.**

Then:

**Start a continuous infusion of 40 ml (8.8 mmol) of calcium gluconate 10% in 1 litre of sodium chloride 0.9% or glucose 5% over 24 hours.**

# Management of Hyponatraemia

- Early symptoms include: anorexia, lethargy, and nausea. Late symptoms include: agitation, seizures, focal neurology, and coma. Symptom severity depends on speed of onset.
- Initial assessment should include:
  - Presenting complaint and past medical history: GI losses, heart / liver failure, malignancy, endocrine causes.
  - Clinical assessment of fluid status: is patient fluid overloaded or fluid depleted?
  - Medication review e.g. diuretics, ACE inhibitors, antidepressants, anti-convulsants, and review others in BNF.

**Plasma Sodium (Na) level**

**Na < 130 mmol/L**

Check:

- Serum and urine osmolality and urinary Na
- Glucose, TFT, CXR, SST, myeloma screen and breast examination as appropriate

**Na > 130 mmol/L**

Monitor Na and fluid balance

**Serum Osmolality**

**Serum Osmolality > 285 mmol/L**

Pseudo-hyponatraemia (causes: lipids / paraproteins / ethanol)

**Serum Osmolality < 285 mmol/L**

**Potential causes of serum osmolality < 285 mmol/L (depending on urinary Na and fluid status)**

| | Hypovolaemic | Euvolaemic | Hypervolaemic |
|---|---|---|---|
| **Urinary Na < 20 mmol/L** | GI loss<br>Fluid shift (e.g. pancreatitis)<br>Burns | Acute water overload<br>Malnutrition | Liver cirrhosis<br>Cardiac failure<br>Nephrotic syndrome |
| **Urinary Na > 20 mmol/L** | Diuretics<br>Adrenal Insufficiency (mineralocorticoid)<br>Salt-wasting<br>Nephropathy<br>Cerebral salt-wasting | Drugs (e.g. antidepressants)<br>Renal failure<br>Hypothyroidism<br>Pituitary insufficiency<br>SIADH* | |

Restore volume with **isotonic sodium chloride IV 0.9%.**[#]

**Only use hypertonic sodium chloride on the advice of the consultant.**

With senior's advice:

- Stop relevant medications
- Fluid restrict to 1.5 L/day
- Treat underlying cause
- Consider sodium chloride IV if symptomatic[#]
- Consider demeclocycline / vasopressin antagonists (only on consultant advice)

**If stable and asymptomatic, no action may be required.**

**Note: *SIADH:** serum osmolality < 285 mmol/L, with inappropriately high urinary sodium and osmolality; renal / adrenal / pituitary / cardiac causes excluded and not dehydration or medication-related.

[#]Rate of Na correction should not exceed 2 mmol/L/hr or 12 mmol/L in 24 hours, to avoid central pontine myelinolysis.

# Management of Hypernatraemia

Serum Na >145 mmol/L can be caused by reduced water intake (dehydration), or where water losses are greater than sodium losses (e.g. watery diarrhoea).

## Assessment / Monitoring

- There are no specific clinical features of hypernatraemia. It is usually diagnosed incidentally on serum testing. Also check other biochemical indices such as renal failure, hyperglycaemia and hypercalcaemia.
- Identify underlying cause of hypernatraemia. Consider measuring urine osmolality.
  - Urine osmolality < plasma osmolality – look for diabetes insipidus
  - Urine osmolality > plasma osmolality – look for osmotic diuresis / heatstroke, etc.
- If patient is also hypovolaemic, then monitor urinary output and renal function.

## General Management

- Treat underlying cause once identified. This is as important as treatment of hypernatraemia.
- Mild cases of hypernatraemia – replace missing body water with oral water (not electrolyte drinks) or glucose 5% IV.
- Severe cases of hypernatraemia (e.g. Na > 170 mmol/L) - give glucose 5% IV unless the patient is volume depleted and hypotensive, in which case give sodium chloride 0.9% IV. It is important that the rate of reduction of serum Na does not occur more rapidly than about 10 mmol/L per day.
  - Reassess and record patient's blood results and clinical conditions every 8 hours. Recheck serum Na after 2 L of fluid replacement, or after 8 hours at the latest.
  - Patients should be handed over to the next shift to clarify monitoring and fluid requirements.
- If diabetes is simultaneously present, then BM monitoring is required and if the blood glucose is > 30 mmol/L then follow HONC guideline (page 279).
- In complex cases, the free water deficit can be calculated and advice can be sought from Biochemistry physicians, to guide the rate of water replacement.

Section 10

# Musculoskeletal and Joint Disease

# Management of Gout

## Introduction

Gout is a common condition encountered in both hospital inpatients and primary care particularly in men. It is due to the deposition of uric acid in the joints and periarticular tissues.

First attacks of gout commonly present as monoarthritis, but polyarticular presentations and chronic tophaceous gout may also be encountered.

Risk factors for gout include: hyperuricaemia (note: most people with hyperuricaemia never suffer an attack of gout), obesity, excess alcohol (especially beer), renal impairment, metabolic syndrome (hypertension, hyperlipidaemia, diabetes mellitus (type 2)).

More information can be found at:

www.rheumatology.org.uk/resources/guidelines/bsr_guidelines.aspx

## Assessment / Monitoring

The differential diagnosis can be septic arthritis or pseudo-gout (pyrophosphate arthritis). Check:

- Urate level. This can sometimes fall during an acute attack, so if the level is normal, then repeat once the acute attack has resolved.
- U&Es / LFTs, consider glucose / lipids
- Joint aspiration (large joints) for gram stain, culture and microscopy for urate crystals. This is not needed if diagnosis has previously been established and there is no suspicion of septic arthritis.
- X-ray feet. In > ¾ of patients first attack is in the first metatarsophalangeal joint, and this joint is involved at some stage in 90% of cases.

## General management

### Lifestyle Modifications

Patients should be advised to:

- Reduce alcohol consumption
- Modify diet to achieve ideal body weight
- Address cardiovascular risk factors

*Continues on next page*

# Treatment options

## Management of acute attack

- **Non-Steroidal Anti-Inflammatory Drug (NSAID) (see next page for details)**

  **or**
- **Colchicine oral 500 micrograms 2 - 3 times daily (stop if diarrhoea develops).** Courses exceeding 6 mg in total are unlicensed but may be appropriate. Seek specialist advice.

  **or**
- **Prednisolone oral 7.5 mg - 15 mg each day for 3 - 5 days only and discuss with rheumatology.**

  **or**
- Intra-articular steroid – useful for monoarthritis after infection excluded by negative synovial fluid culture (discuss with rheumatology).

Allopurinol should be initiated only once an acute attack has settled **but** if acute attack occurs in a patient already receiving allopurinol, **do not stop allopurinol.**

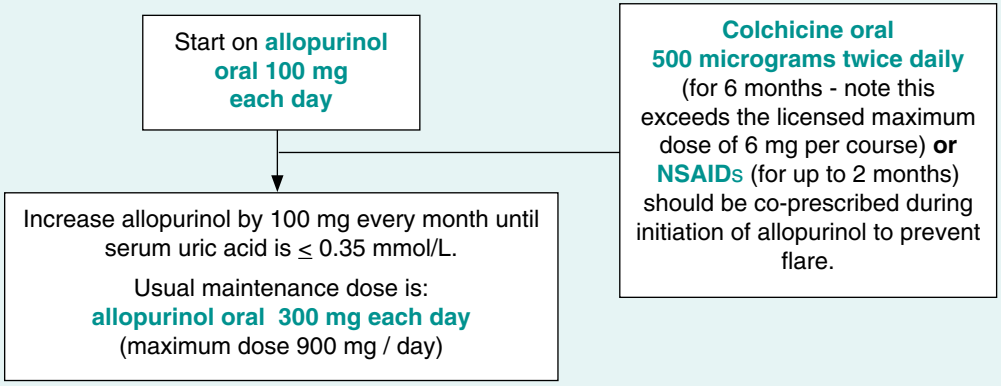
## Long-term management of gout

Long-term uric acid lowering therapy will be required for patients with:

- > 3 attacks in 1 year *or*
- Gouty tophi *or*
- Urate renal calculi *or*
- Radiological damage (erosions) secondary to gout *or*
- Serum urate > 0.6 mmol/L

Allopurinol should be initiated only once an acute attack has settled (see below). In patients whose uric acid levels have failed to respond adequately despite optimal dosing of allopurinol or those who are intolerant, an alternative is:

**Febuxostat oral 80 mg daily (increased to 120 mg daily after 4 weeks if the serum urate still exceeds 0.36 mmol/L).** As with allopurinol, prophylaxis for flares of gout should continue for the first 6 months of treatment (see below). Febuxostat is **not** recommended for patients with ischaemic heart disease or heart failure.



# Management of Arthritis

## Introduction

This section covers the first-line management of patients with:

- Osteoarthritis
- Inflammatory arthritis e.g. rheumatoid arthritis, psoriatic arthritis, reactive arthritis, spondyloarthropathy, crystal arthritis

More information can be found at:

www.rheumatology.org.uk/resources/guidelines/bsr_guidelines.aspx

## Assessment / monitoring

Refer to rheumatology services for further advice regarding the assessment and management of patients with inflammatory arthritis and in cases where there are diagnostic difficulties. This should be done as soon as possible after presentation.

This section does not address the management of septic arthritis. All cases of suspected septic arthritis should be referred to rheumatology or orthopaedics depending on local protocol.

## General management

- Exercise – all patients should receive physiotherapy advice regarding joint protection, exercise and occupational therapy input.
- Weight control – all patients should receive advice regarding maintaining ideal body weight.

## Treatment options

### A. Pain control

#### 1. Non-opioid and weak opioid analgesics

**Paracetamol oral 1 g 4 - 6 hourly (maximum 4 g in 24 hours)**

- Paracetamol is as effective as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) in many patients with osteoarthritis. Consider dose reduction of paracetamol in patients with low body weight (≤ 50 kg), renal / hepatic impairment or glutathione deficiency (chronic malnourishment, chronic alcoholism) to 15 mg/kg/dose up to four times daily (max 60 mg/kg/day). An example is: dose reducing to **paracetamol oral 500 mg four times daily**.
- If response is inadequate to simple analgesia, NSAIDs may be tried but should be stopped if ineffective.

**2. NSAIDs** (also see Anti-inflammatory guidelines, Clinical Guideline Electronic Resource Directory and search in musculoskeletal and joint diseases section)

**Ibuprofen oral 400 mg - 600 mg three times daily after food**

**or**

**Naproxen oral 250 mg - 500 mg twice daily after food**

**Continues on next page**

**Treatment options continued**

NSAIDs are associated with risk of significant toxicity, and the following should be noted:

- Always use the lowest possible dose of NSAID for the shortest possible duration.
- **Never** use combinations of NSAIDs.
- NSAIDs are contraindicated in renal failure, cardiac failure and active peptic ulcer disease.
- Consider gastroprotection in those patients at increased gastrointestinal (GI) risk (see Table 1). Remember patients remain at risk of perforation and bleeds despite gastroprotection.
- Avoid or minimise use of NSAIDs in patients with ischaemic heart disease and hypertension.
- Co-administration of ibuprofen and aspirin negates the antiplatelet effects of aspirin and should be avoided. Instead, aspirin should be taken first thing in the morning, approximately 1 hour before ibuprofen.

**Table 1 – People at high risk of serious NSAID induced GI adverse effects**

- Age ≥ 65 years
- History of gastroduodenal ulcer, perforation or GI bleeding.
- Concomitant use of medication known to increase risk of upper GI adverse events e.g. aspirin, anticoagulants, corticosteroids, selective serotonin re-uptake inhibitors.
- Serious co-morbidity e.g. cardiovascular disease, renal or hepatic impairment, diabetes, hypertension.
- Requirement for prolonged duration of NSAID use.
- High dose NSAID use (ibuprofen 2400 mg per day or naproxen 1 g per day).

## Gastroprotection

- **Proton pump inhibitors e.g.:**

  **Omeprazole oral 20 mg each day or**

  **Lansoprazole oral 15 mg - 30 mg each day.**
- Gastroprotection is only required for the duration of the NSAID course.

## COX-2 selective NSAIDs (Coxibs)

**Choice: Celecoxib oral 100 mg twice daily or etodolac oral 600 mg daily** (in 1 -2 divided doses).

Coxibs are associated with less GI toxicity than NSAIDs but with increased cardiovascular risk. The following should be noted:

- Coxibs should only be prescribed for patients with high risk of GI toxicity and low cardiac risk.
- Coxibs should not be prescribed for patients taking concomitant aspirin.
- For patients requiring a proton pump inhibitor, a traditional NSAID should be used in preference to a Coxib.

**Continues on next page**

**Treatment options continued**

## B. Disease Modifying Anti-Rheumatic Drugs (DMARDs) and immunosuppressant therapies

Many patients with inflammatory arthritides or connective tissue diseases will be receiving one or more DMARDs or immunosuppressants including biologic agents such as tumour necrosis factor-alpha (TNF α) inhibitors. These medicines are usually initiated on the advice of rheumatology.

DMARDs include:

- Methotrexate (once weekly preparation, orally or subcutaneously)
- Sulfasalazine EC
- Hydroxychoroquine
- Gold
- Leflunomide
- Azathioprine
- Ciclosporin

Guidelines on DMARD monitoring (BSR / BHPR) are available at:

www.rheumatology.org.uk/resources/guidelines/bsr_guidelines.aspx

Biologics include:

- Etanercept (SC, once or twice weekly)
- Adalimumab (SC, once a fortnight)
- Infliximab (IV, usually in day-ward setting)
- Rituximab (IV, usually in day-ward setting)
- Tocilizumab (IV, once every 4 weeks)
- Abatacept (IV, initially fortnightly then once every 4 weeks)
- Certolizumab (SC, once a fortnight)
- Golimumab (SC, once a month)

Toxicity:

These drugs may increase the patient's risk of infection and/or mask the typical signs of sepsis. Withhold these drugs and discuss with rheumatology if:

- Infection is suspected on treatment with DMARDs or immunosuppressants.
- Changes to DMARD doses are planned when a patient is admitted for other reasons.
- Long-term therapies stopped.
- A DMARD prescription is unclear - withhold drug until it has been discussed.

Section 11

# Palliative Care

# Pain Management in Palliative Care

The full set of guidelines in this section are available as A5 booklets from the palliative care team and A4 folders on all wards. For patients with heart failure requiring palliative care see "Living and Dying in Advanced Heart Failure: A Palliative Care approach" on www.palliativecarescotland.org.uk

## Analgesic Step Ladder (see table on page opposite)

Assess pain fully before treatment (see pain assessment in full guidelines). Ask the patient regularly about their pain. Use a pain assessment tool and record pain scores. Prescribe regular analgesia for continuous pain. Discuss and resolve any concerns of the patient about taking opioids.

- Movement / incident related or episodic pain – a dose of short-acting opioid before moving or when pain occurs may help. Seek advice as it can be difficult to manage.
- Constipation – With opioids give regular laxatives (see page 45 for choice). Also further information can be found in either the palliative care booklet or in the A4 folders on the wards.
- Nausea and vomiting – Prescribe antiemetics (metoclopramide or haloperidol) as required for 5 – 10 days.

## Adjuvant Therapies

- NSAID for bone pain, liver pain, soft tissue infiltration, or inflammatory pain. Side effects include gastrointestinal ulcers / bleeding (consider proton pump inhibitor), renal impairment, fluid retention. NSAIDs should be used with caution in renal failure and are not advised in myeloma patients.
- Antidepressant or anticonvulsant for nerve pain e.g.
  - **Amitriptyline (unlicensed indication) initial oral dose 10 mg at night. Slowly dose titrate up every 5 to 7 days, if required to a maximum of 75 mg at night.**
  - **Gabapentin initial oral dose 100 mg to 300 mg at night then titrate dose every few days to 300 mg three times daily.** Seek advice if dose requires escalation higher than 300 mg three time daily. Consider a lower dose and slower titration for the frail / elderly / patients with renal impairment.

  There is no clear difference in efficacy between these preparations. See BNF for side effects.
- Dexamethasone for intracranial, nerve or liver pain but dose varies:
  - Intracranial pressure – **dexamethasone oral 16 mg each morning**
  - Nerve pain – **dexamethasone oral 12 mg each morning**
  - Liver pain – **dexamethasone oral 4 mg to 8 mg each morning.**

  Reduce to the lowest effective dose.
- For TENS, nerve block, radiotherapy, surgery, bisphosphonates, ketamine seek specialist advice.

## Analgesic Step Ladder

### Step 1: Mild Pain

**Paracetamol oral 1 g four times a day** or NSAID (if not contraindicated) +/- other adjuvant (see previous page)

**N.B.** Consider dose reduction in patients ≤ 50 kg, renal / hepatic impairment or glutathione deficient (chronic malnourishment, chronic alcoholism) to 15 mg/kg/dose (max. 60 mg/kg/day). An example is: reduce dose to paracetamol oral 500 mg four times daily.

### Step 2: Mild to moderate pain

| Opioid | + | Paracetamol (dose as in Step 1) | or | NSAID (if not contraindicated) | +/- | other adjuvant (see previous page) |
|---|---|---|---|---|---|---|
| **codeine or dihydrocodeine oral 30 – 60 mg four times a day** | | | | | | |

Can use combination preparations e.g.
**Co-codamol oral 30/500 mg 2 tablets four times a day**

### Step 3: Moderate to severe pain

| Opioid (first line is morphine) | + | Paracetamol (dose as in Step 1) | or | NSAID (if not contraindicated) | +/- | other adjuvant (see previous page) |
|---|---|---|---|---|---|---|

- *Stop any step 2 opioid*
  (codeine / dihydrocodeine 240 mg/24 hours ≈ morphine oral 30 mg/24 hours)
- If commencing with immediate release oral morphine give 5 mg every 4 hours and as required for breakthrough pain. Use lower doses and increase slowly if patient is frail, elderly or has renal impairment. Convert to modified release morphine when stable by dividing total daily dose of immediate release morphine by 2, then prescribing the dose as oral morphine modified release 12 hourly. Also prescribe for breakthrough pain (see fifth point, below).
- If starting patient with modified release oral morphine give 10 – 15 mg twice a day and immediate release morphine 5 mg as required for breakthrough pain. Use lower doses and increase slowly if patient is frail, elderly or has renal impairment.
- Dose titration: increase regular oral morphine dose each day by around 30% (or according to the breakthrough doses used) until pain is controlled or side effects develop. Also increase laxative dose as needed (see page 45 for choice).
- Breakthrough pain - prescribe immediate release morphine at 1/6th of the regular 24 hour oral morphine dose, as required. Assess 30 – 60 minutes after a breakthrough dose and if pain persists then give a second breakthrough dose.
- When to seek advice – see next page

*Continues on next page*

## Subcutaneous analgesia

Calculate the 24 hour dose of oral morphine administered. Convert this dose to morphine SC to be given in a syringe pump over 24 hours (see next page for dose conversions).

For breakthrough pain prescribe 1/6th of the 24 hour SC opioid dose as required.

## Pain not controlled

Seek advice if:

- Pain is not responding to treatment.
- Dose of opioid rapidly increased but patient still in pain.
- Episodes of acute severe pain.
- Pain worsens on movement.

## Opioid toxicity – seek advice

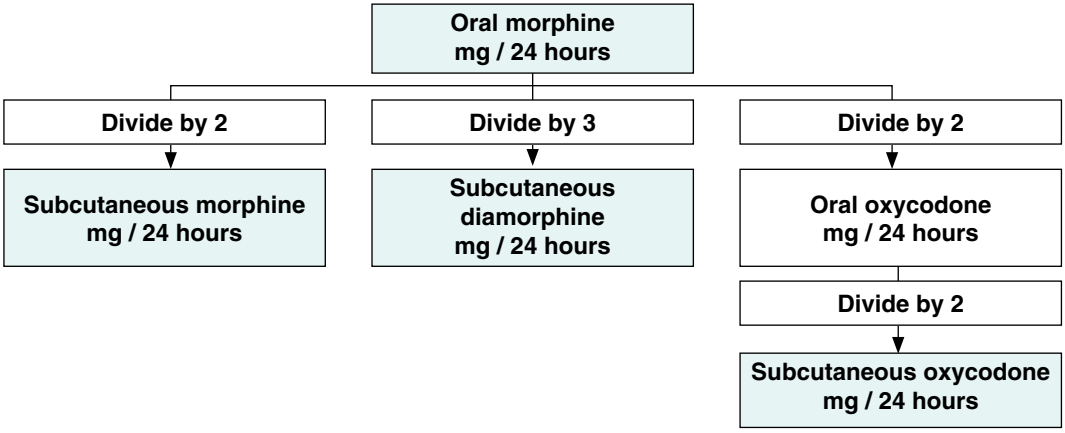
- Signs include:
  - Increasing drowsiness / sedation
  - Vivid dreams / hallucinations / delirium
  - Muscle twitching / myoclonus / jerking
  - Abnormal skin sensitivity to touch
- Reduce opioid dose by 1/3, ensure patient is well hydrated; review and re-titrate the analgesia.
- Consider adjuvant therapies and/or alternative opioids.
- Naloxone (in small titrated doses) is only needed for life-threatening respiratory depression (page 41).

# Opioid Conversion Chart

This is advice on conversion factors and calculations to estimate equivalent doses of different opioids. It is **not** a guideline on using opioids. **If converting in the opposite direction multiply rather than divide.**

**N.B.** Consider reducing final opioid dose by a further one third when changing to a different opioid; monitor for breakthrough pain and toxicity when switching opioids. Titrate dose up and down according to efficacy and side effects. Contact Palliative Care Team for advice.

## Opioid Conversion Chart




## Renal Impairment

Morphine and oxycodone are contraindicated in patients with eGFR < 60 ml/minute/1.73m$^2$. Contact local palliative care team for advice on alternative opioids.

## Other opioids

Contact local Palliative Care Team or pharmacy for further information on other opioids e.g. alfentanil, hydromorphone.

## Breakthrough pain

- For **same** opioid and route: divide 24 hour opioid dose by 6.
- For fentanyl patch: See guidance below.
- Consider increasing the breakthrough opioid dose as the background opioid dose increases.

Fentanyl products which are licensed for fast onset / short duration breakthrough cancer pain should only be prescribed under a palliative medicine specialist's supervision. Patients must be on a background opioid.

For general guidance on fentanyl patches, see below. More detailed information is available at www.palliativecareggc.org.uk and in the Fentanyl guideline in the Palliative Care booklet from the Palliative Care Team or A4 folder on the ward.

*Continues on next page*

## Good prescribing points for transdermal fentanyl

Indications for using fentanyl patches:

- Stable pain only, not suitable for acute pain.
- Oral route not viable due to e.g. poor absorption or swallowing difficulties e.g. ileostomy, head and neck cancer, etc.
- Morphine and other oral strong opioids cannot be tolerated due to side effects e.g. confusion, excessive ongoing drowsiness, intractable constipation.
- Compliance issues – a supervised patch change will assist this.

**Remember:**

- Pain **must** be stable:
  - It takes 6 - 12 hours for the patch to begin to work and will take 36 - 48 hours to reach stable plasma levels (do not increase patch before 72 hours have passed).
  - Any subsequent dose increase will take 48 hours to see full therapeutic effect.
- Fentanyl is a **potent** opioid, 100 - 150 times more potent than oral morphine.
- Fentanyl patches are not normally appropriate in opioid naive patients and great care is required in this situation. Seek specialist advice.

  **Note:** Durogesic DTrans® 12 micrograms/hour is only licensed for fine titration between 25 and 75 micrograms/hour. Initiating a patient on a 12 microgram/hour patch will be an 'off-label' use. There will be clinical situations when this may be justified.
- As patches vary considerably in their appearance and to avoid the risk of patient confusion, patients should not be changed from one formulation or make to another without adequate counselling.
- If the patient, on a fentanyl patch, is dying and/or pain control becomes unstable and additional analgesia is required, **do not take the patch off**. Leave the patch on (continuing to replace every 72 hours) and add a continuous subcutaneous infusion.
- There is a very wide range in equivalency between transdermal fentanyl and oral morphine.

# Palliative Care – Symptoms

See BNF, Prescribing in Palliative Care: www.palliativecareggc.org.uk
and www.palliativecareguidelines.scot.nhs.uk

| Palliative Care Symptoms | Important notes / comments to consider before prescribing | Therapeutic choice |
|---|---|---|
| Dry mouth | Encourage good oral hygiene with regular sips of water before considering saliva replacement. | Saliva replacement gel e.g. Biotène Oralbalance® - use as required.<br>See Oral Hygiene Policy. |
| Excessive respiratory secretions | Hyoscine butylbromide is a less sedating alternative.<br>Hyoscine hydrobromide can cause sedation. | Hyoscine butylbromide<br>SC bolus 20 mg hourly as required (max 120 mg / day)<br>**or**<br>SC infusion 60 - 120 mg over 24 hours |
| | | Glycopyrronium bromide<br>SC bolus 200 micrograms 6 - 8 hourly as required<br>**or**<br>SC infusion 600 -1200 micrograms over 24 hours |
| | | Hyoscine hydrobromide (**N.B.** Sedating)<br>SC bolus 400 micrograms every 2 hours as required (max 2400 micrograms/day)<br>**or**<br>SC infusion 1200 - 2400 micrograms over 24 hours |

Table continues on next page

Table continued from previous page

| Palliative Care Symptoms | Important notes / comments to consider before prescribing | Therapeutic choice |
|---|---|---|
| Restlessness | Assess for cause and reverse as appropriate.<br>Haloperidol and levomepromazine have long half-lives and can either be given as SC infusion or as SC bolus.<br>Levomepromazine can cause sedation and hypotension. | Midazolam (anxiety / distress)<br>SC infusion, initial starting dose 5 mg, titrate up to 10 - 60 mg over 24 hours.<br>**or**<br>SC bolus 2 mg - 5 mg hourly as required (max 6 doses in 24 hours). |
| | | Haloperidol (confusion / delirium)<br>SC infusion, initial starting dose 2 mg – 5 mg over 24 hours. Titrate according to response.<br>**or**<br>SC bolus, 2 mg - 5 mg in one to two divided doses. |
| | | Levomepromazine (confusion / agitation)<br>**N.B**. Sedating<br>SC infusion, initial starting dose 2.5 mg - 12.5 mg over 24 hours. Titrate according to response.<br>**or**<br>SC bolus 2.5 mg - 12.5 mg in one to two divided doses |

Table continues on next page

Table continued from previous page

| Palliative Care Symptoms | Important notes / comments to consider before prescribing | Therapeutic choice |
|---|---|---|
| Nausea and vomiting | Use guidelines to identify possible causes and suitable treatments (see www.palliativecareggc.org.uk)<br><br>Prescribe regularly until symptoms controlled.<br><br>If vomiting regularly, switch to SC route, ideally administer via syringe pump over 24 hours.<br><br>Avoid pharmacologically antagonistic combinations e.g. cyclizine and metoclopramide.<br><br>Metoclopramide: use with caution in young, especially female patients, because of risk of extrapyramidal side effects.<br><br>In intractable nausea and vomiting, low dose levomepromazine is used as second line treatment. The 6 mg tablet is an unlicensed preparation and may be available from your hospital pharmacy. Advice about its use should be obtained from the Palliative Care team. | Treatment option: see Nausea and Vomiting Guideline (palliative care booklet or folder on ward).<br><br>Prophylactic antiemetics may be necessary (when opioid initiated and/or opioid dose increased):<br><br>Prescribe:<br>Metoclopramide oral 10 mg 8 hourly, increased to 20 mg 6 hourly (caution with certain patient groups)<br><br>**or**<br><br>Haloperidol oral 0.5 - 3 mg at night |

# Palliative Care – Last days of life

When all reversible causes for the patient's deterioration have been considered, the multi-disciplinary team agrees the patient is dying and changes the goals of care. Reversible causes to consider include: dehydration, infection, opioid toxicity, renal impairment, hypercalcaemia or delirium. Clinical signs may include: patient is bedbound, increasingly drowsy or semi-comatose, only able to take sips of fluid or has difficulty swallowing tablets.

## Management of a dying patient and their family

Plan and document care; consider using a care pathway or checklist.

- Discuss prognosis (patient is dying), goals of care (maintaining comfort) and preferred place of care.
- If discharge home is possible, prompt and careful planning is needed. Contact GP, district nurse and occupational therapist urgently.
- Clarify resuscitation status; check DNA CPR form has been completed (see national policy). Reassure the patient and family that full supportive care will continue.
- Discontinue inappropriate interventions (blood tests, IV fluids and medication, vital signs monitoring, frequent blood sugar tests).

## Hydration

- Discontinue tube feeding / fluids if respiratory secretions present, if there is a risk of aspiration due to reduced conscious level or at the patient's request.
- Over-hydration contributes to distressing respiratory secretions. Artificial fluids are usually not appropriate, but if indicated can be given subcutaneously.

## Symptom control in the last days of life

### Anticipatory prescribing

In all patients the following should be prescribed in the "when required" section of the kardex:

- Opioid analgesic SC, hourly: dose depends on patient, clinical problem and previous opioid use. Prescribe 1/6th of 24 hour dose of any regular opioid or if not on a regular opioid prescribe, **morphine SC 2 mg hourly**.
- Anxiolytic sedative: **midazolam SC 2 mg to 5 mg hourly**.
- Anti-secretory medication: **hyoscine butylbromide (Buscopan®) SC 20 mg hourly**.
- Antiemetic: **haloperidol SC 500 micrograms 12 hourly or levomepromazine SC 2.5 mg to 5 mg 12 hourly**.

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## Management of symptoms present in last days of life

**Pain:**

- Non-opioid analgesics: Paracetamol or diclofenac (liquid / dispersible / rectal preparations). NSAID benefits may outweigh risks in a dying patient; can help bone, joint, pressure sore, inflammatory pain.
- Opioid analgesics: Convert any regular oral morphine or oxycodone to a 24 hours SC infusion – see opioid conversion flowchart on page 319 and/or seek advice. Continue fentanyl patches in dying patient, see page 320. For breakthrough pain, prescribe dose hourly as required by:
  - Calculating 1/6th of the 24 hour of any regular oral or SC opioid
  - If not on regular opioid, prescribe **morphine SC 2 mg**

**Agitation / delirium:**

- Anxiety / distress – **Midazolam SC 2 mg to 5 mg hourly as required**
- Confusion / delirium – **Haloperidol SC 2 mg once or twice daily**
- Established terminal delirium / distress –

  First-line: **Midazolam SC 20 mg to 30 mg over 24 hours in a syringe pump + midazolam SC 5 mg hourly as required**

  Second-line: Refer to palliative care guidelines (see link below), local palliative care team or seek senior medical advice.

**Nausea / Vomiting:**

If already controlled with an oral antiemetic, use the same drug as a SC infusion. Treat new nausea / vomiting with a long-acting antiemetic given by SC injection or give a suitable antiemetic as a SC infusion in a syringe pump. Long-acting antiemetics include:

- **Haloperidol SC 1 mg 12 hourly or 2 mg once daily**
- **Levomepromazine SC 2.5 mg 12 hourly or 5 mg once daily**

For antiemetic doses in SC infusion see the Palliative Care A5 booklets available from the Palliative Care Team or refer to the A4 folders on the wards or access: www.palliativecareguidelines.scot.nhs.uk. For persistent vomiting, a nasogastric tube, if tolerated, may be better than medication.

**Respiratory tract secretions:**

Avoid fluid overload; assess fluid balance, stop IV/SC fluids and tube feeding. Changing patient's position may help. Intermittent SC injections often work well or medications can be given as SC infusions (see page 321)

For information on management of other symptoms in the patient's last days of life, see Palliative Care guideline available as A4 folder on all wards, or A5 booklets can be obtained from the Palliative Care team or access www.palliativecareguidelines.scot.nhs.uk.

Section 12

# Oncological Emergencies

# Management of acute oncological complications

## Introduction

Patients with locally advanced or metastatic cancer will often present as an emergency with acute complications of their disease or treatment. Some patients will have a known diagnosis of cancer and others may present with acute complications of undiagnosed malignant disease. Listed below are common oncological emergencies with guidance on signs and symptoms and initial management. In all cases, the on-call oncology or haematology registrar should be paged urgently.

As with all newly admitted patients, a thorough drug history should be taken. This is especially important for cancer patients presenting with acute toxicity from chemotherapy or other systemic anticancer therapy. Any oral anticancer therapy should be identified and discontinued until advice is sought from the on-call oncology / haematology registrar.

**This section includes advice on management of:**

- Malignant spinal cord compression (see next page)
- Raised intracranial pressure in cancer patients (page 331)
- Tumour lysis syndrome (page 334)
- Malignant ascites (page 336)

**Other oncological complications are covered elsewhere in the Handbook:**

- Neutropenic sepsis: see infection section page 214.
- Superior vena cava obstruction (SVCO page 155), stridor (page 153) and malignant pleural effusion (page 145) in respiratory section.

Hypercalcaemia of malignancy: see page 304 and West of Scotland guideline on the use of bisphosphonates in cancer patients www.intranet.woscan.scot.nhs.uk / Systemic Anti Cancer Therapy Protocols / Supportive Care).

# Malignant Spinal Cord Compression (MSCC)

N.B. West of Scotland guidelines on MSCC are available in the Protocols and Clinical Guidelines section of www.beatson.scot.nhs.uk

## Introduction

MSCC is most common in, but not exclusive to, patients with lung cancer, breast cancer, prostate cancer and myeloma, as well as patients with known bony metastases. For patients not known to have cancer, MSCC can be the first presentation. Early identification and referral of patients with MSCC is crucial for optimal patient outcomes.

MSCC is an oncological emergency and should be suspected in any patient with a known cancer diagnosis and suggestive symptoms (as described below). It should be discussed with a Registrar immediately, and with on-call Oncology Registrar as soon as possible.

## Signs and Symptoms

- Pain is usually the first presenting symptom and has often been present for a number of weeks before MSCC is diagnosed.
- Pain may be new, or may present as a significant change in the character of longstanding pain. Pain is usually in the back but can be radicular, often described as a tight band around the chest or abdomen.
- Later presenting symptoms are motor deficits (e.g. muscle weakness, loss of coordination, paralysis), sensory deficits (e.g. paraesthesia, loss of sensation) or autonomic dysfunction (bladder or bowel problems).You should always enquire about bowel and bladder dysfunction in patients presenting with leg weakness.

## Assessment / Monitoring

If MSCC is suspected:

- Clinical assessment and examination, including full neurological examination and assessment for a sensory level. A spastic paraparesis is the typical finding but it is not always clear cut.
- Contact the oncall Oncology Registrar ASAP.
- Urgent MRI of the whole spine (within 24 hours).
- Consider Neurosurgical referral (e.g. unstable or high spinal lesion, unknown primary).

## Treatment

**Immediate:**

- Give **dexamethasone oral 8 mg as a single dose** as soon as MSCC is suspected, and whilst waiting for MRI, followed by **dexamethasone 8 mg twice daily (morning and lunchtime)**. Use IV route if oral contraindicated.
- Consider prophylactic gastroprotection whilst patient on high dose steroids (**omeprazole oral 20 mg daily or lansoprazole oral 30 mg daily**).

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- Pain control.
- Keep flat until stability of spine is known (following MRI).
- Urgent radiotherapy (within 24 hours of MRI diagnosis), chemotherapy (and/or surgery) depending on radiosensitivity / chemosensitivity of the culprit tumour. Most common treatment is radiotherapy. Contact on-call Oncology Registrar.
- Thromboprophylaxis (if appropriate)

**When patient is stabilised:**

- Physiotherapy and occupational therapy referral – on day of admission
- Palliative Care referral
- Patient / care / family information and psychological care

# Raised intracranial pressure in cancer patients

## Introduction

For patients with malignancy the principle causes of raised intracranial pressure (ICP) will be the presence of space-occupying tumours or obstructive hydrocephalus. It should not be forgotten however that rarely other causes (such as hypertension, head injury, non-tumour space-occupying lesions (such as abscess) or excess cerebral spinal fluid production) may be the cause and require additional expertise. Cardinal features are headache and vomiting which may be associated with hypertension and bradycardia. Fundoscopy may be helpful, showing papilloedema and loss of retinal venous pulsation. In extreme situations there may be depression of consciousness, false localising signs and pupillary abnormalities suggesting imminent coning.

## Treatment / drug therapy

### Emergency

In an emergency situation if the history and clinical signs indicate imminent coning, nurse the patient in a position with head elevated and give:

**Dexamethasone IV 8 mg and repeat 4 hourly if needed.**
Consider prophylactic gastroprotection whilst patient on high dose corticosteroids.

When the situation is under control manage as below.

### Urgent

If the clinical diagnosis is clear but the cause is not established, an emergency CT (or MRI) scan is indicated – if out-of-hours, discuss with a senior member of the team. This should be performed with and without contrast and the result discussed with the radiologist without delay.

Treatment depends on cause:

- One or more intracranial mass lesions causing pressure

  Tumour: ..... Is there a therapeutic option? ..... Yes..... Go to A

  No ..... Go to C

  Non tumour (e.g. abscess)..... Go to D
- Obstructive hydrocephalus..... Go to B
- Brain Swelling or ventricular enlargement of unknown cause..... Go to D

### A. Stabilising the condition to allow a therapeutic option

1. Nurse patient with head of bed elevated
2. Ensure adequate analgesia – use subcutaneous route if patient is vomiting.

   Prescribe adequate analgesia (see page 316). Pain of raised ICP can be extremely severe.

**Continues on next page**

**Treatment /drug therapy continued**

3. Administer corticosteroid

   **Dexamethasone IV 8 mg. If the patient responds, is stable and not vomiting then continue with dexamethasone oral 4 mg four times daily.**

   If the patient remains unwell or continues to vomit then continue with IV dexamethasone. **Doses of up to dexamethasone IV 8 mg 3 - 4 hourly can be given for up to 2 - 3 days if needed.**

   Consider prophylactic gastroprotection whilst patient on high dose corticosteroids **(omeprazole oral 20 mg daily or lansoprazole oral 30 mg daily)**.

4. If the patient still does not respond then try mannitol IV – seek advice from a senior colleague. Long-term mannitol is contrainidicated.

   **Mannitol total dose is 1 g/kg. First give 100 ml of a 20% solution (20 g mannitol) over 15 minutes. Then give the remainder over approximately 45 minutes.** Repeat the following day if required but not long-term.

   Example: For a patient weighing 60 kg, give 100 ml of 20% mannitol (20 g) over 15 minutes and then 200 ml of 20% mannitol (40 g) over 45 minutes.

5. For nausea and vomiting give:

   **Cyclizine SC 100 mg to 150 mg over 24 hours via syringe driver.**

6. Beware of seizure threshold and ensure antiepileptic medication is continued – switch oral to parenteral if patient vomiting (see palliative care guidelines for seizure control at www.palliativecareguidelines.scot.nhs.uk)

7. Refer for definitive therapy (surgery, radiotherapy)

### B. Patient requires a shunt to stabilise

Manage as A (but do not give mannitol) and contact neurosurgeons urgently requesting opinion on shunt placement.

### C. Palliative care only (no longer-term management option)

1. If there is no therapeutic option then corticosteroids can still be tried for symptom relief. See above for initial dosing of dexamethasone. Doses greater than 16 mg of dexamethasone should rarely be used.

2. Analgesics – see page 316 for guidance. Patients terminally ill with raised ICP may need high doses of opiates. Consider a non-steroidal anti-inflammatory medicine e.g. **Diclofenac which may be given SC via syringe driver (150 mg over 24 hours).**

3. Anti-emetics – Try **cyclizine 100 mg to 150 mg SC over 24 hours via syringe driver.**

4. Sedation. Patients may be agitated for a variety of reasons. Benzodiazepines, mostly midazolam SC, are a standard approach to sedation. (for more information see palliative care guidelines at www.palliativecareguidelines.scot.nhs.uk).

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**Treatment /drug therapy continued**

5. Give analgesics, anti-emetics and sedatives by continuous SC infusion – see Palliative Care section pages 318 - 325. Also be aware of syringe driver compatibilities (see palliative care guidelines at www.palliativecareguidelines.scot.nhs.uk).
6. Consider referral to hospital specialist palliative care team.
7. If the patient appears to be in the last days of life, and fits the criteria for the Liverpool Care Pathway (LCP), then this option should be discussed with senior medical staff.

### D. This may well be a condition not directly associated with intracranial tumour

Treat with corticosteroids as in A but do not give mannitol. Contact the neurology or neurosurgical team as appropriate.

# Tumour Lysis Syndrome

This section describes diagnosis and initial management. For advice on prevention refer to local haematology department policy.

## Introduction

Tumour lysis syndrome (TLS) is a potentially fatal syndrome characterised by a group of metabolic derangements caused by the release of cellular components into the blood after rapid lysis of malignant cells. This is seen most often at the initial treatment of a number of high grade malignant haematological disorders and results from the instigation of treatment. However, in a small number of cases, patients can present with TLS prior to initiation of any chemotherapy. Patients at highest risk of TLS include those with high cell-count leukaemias, lymphoblastic lymphoma, bulky diffuse large B cell and Burkitt lymphoma, but less commonly, some non-haematological malignancies may present with TLS e.g. germ cell tumours or small cell lung cancer. Patients with TLS often have a high lactate dehydrogenase (LDH) level.

Seek an urgent haemato–oncology review for patients presenting with clinical and/or laboratory features of TLS.

**Clinical features of TLS reflect associated metabolic abnormalities**

- Acute oliguria and renal failure
- Cardiac rhythm disturbance
- Confusion and seizures
- Nausea and vomiting
- Muscle cramps and tetany

**Laboratory features of TLS**

- Hyperuricaemia
- Hyperkalaemia
- Uraemia
- Hypocalcaemia
- Hyperphosphataemia

**N.B.** Spontaneous TLS prior to the initiation of any chemotherapy is associated with hyperuricaemia but frequently NOT with hyperphosphataemia.

**Table 1: Cairo-Bishop Definition of Laboratory Tumour Lysis Syndrome**

| Element | Value | Change from baseline |
|---|---|---|
| Uric acid | $\geq$ 0.48 mmol/L | 25% increase |
| Potassium | $\geq$ 6.0 mmol/L | 25% increase |
| Phosphorus | $\geq$ 1.45 mmol/L | 25% increase |
| Calcium | $\leq$ 1.75 mmol/L | 25% decrease |

Cairo MS, Bishop M. Tumour lysis syndrome: new therapeutic strategies and classification. Br J Haematology. 2004; 127(1):3-11.
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**N.B.**

- Laboratory TLS = ≥ 2 laboratory changes (as per table on the previous page ) within 3 days before or 7 days after chemotherapy.
- Clinical TLS = laboratory TLS plus one or more of the following that is not directly or probably attributable to a therapeutic agent: increased serum creatinine concentration (> 1.5 x ULN), cardiac arrhythmia / sudden death, or a seizure.

Crystallisation of uric acid in renal tubules can further impair renal function. This is an oncological emergency and warrants aggressive therapy and possibly renal support. Sudden death may result from hyperkalaemia and cardiac arrest.

## Treatment of established TLS (only under supervision of haemato-oncologist)

First page the on-call haematology registrar urgently. Effective management involves the combination of treating specific electrolyte abnormalities and/or acute renal failure. The haematology registrar will advise on use of a loop diuretic e.g. furosemide, and intravenous fluids (up to 4 - 6 L/24hours) to attempt to wash out the obstructing uric acid crystals. Rasburicase should also be prescribed. *This may only be prescribed by the haematology specialist and is highly effective in causing a rapid reduction in serum urate levels.*

Renal support with dialysis or continuous veno-venous haemofiltration can be life saving in these patients. Seek an early renal opinion in all established cases particularly in those with oliguria, persistent hyperphosphataemia and hyperkalaemia.

## Management of electrolyte abnormalities

For treatment of hyperkalaemia and hypocalcaemia (seek specialist advice), refer to pages 296 and 306.

### Hyperphosphataemia

- Phosphate > 2.1 mmol/L (moderate) – Increase hydration. Administer phosphate binder **(calcium acetate oral 1 g three times a day, adjust according to phosphate concentration – usual dose 4 - 6 g daily; max 12 g daily)**
- Phosphate > 2.5 mmol/L (severe) – Urgent renal opinion.

**Uraemia:** early renal opinion in all patients

# Malignant-related Ascites

## Introduction

Ascites is caused by malignancy in approximately 7% of patients. A number of mechanisms exist whereby cancer can cause ascites, and its development is not always synonymous with a diagnosis of peritoneal carcinomatosis. The two main causes observed in the Beatson West of Scotland Cancer Centre are:

1. Peritoneal carcinomatosis secondary to malignancies of ovarian and urological origin. In these cases, accumulation of ascites results from blockage of the draining lymphatic channels and increased vascular permeability.
2. Colonic, gastric, breast, pancreatic, and lung cancers may cause peritoneal carcinomatosis and/or massive liver metastases, which can lead to ascites either because they obstruct / compress portal veins or because they cause liver failure.

## Assessment / Monitoring

### History

- Abdominal pain / discomfort, shortness of breath, early satiety, or nausea and vomiting are often symptoms which lead patients to seek medical attention.
- Weight loss will often be recounted prior to the development of ascites (when weight begins to increase again).

### Examination

- The presence of bulging flanks, a distended / firm abdomen, or an everted umbilicus should lead to percussion for dullness and testing for shifting dullness.

### Investigations

- Positive ascitic fluid cytology to establish the diagnosis of malignancy-related ascites, if this is in doubt e.g. a patient with a history of cirrhosis. The overall sensitivity of cytology for the detection of malignancy-related ascites is 58 - 75%.
- CT or ultrasound can confirm clinical suspicion of ascites, with the latter often used for marking an appropriate site for paracentesis. CT is useful to confirm the mechanism of ascites formation, assessing the peritoneum, portal vein and liver.
- Blood tests include FBC, U&Es, LFTs, and coagulation screen. During paracentesis monitor U&Es daily.
- Send ascitic fluid for investigation to help confirm diagnosis and exclude infection. These include cell count and differential, bacterial culture, albumin (for serum-to-ascites albumin gradient), total protein, glucose, LDH, and cytology (described above). Bacterial culture is particularly important in those with fever or abdominal pain, although it should be noted that peritoneal carcinomatosis can sometimes mimic spontaneous bacterial peritonitis. Initially give antibiotics (see page 238) when an elevated fluid neutrophil count is detected, but discontinue when it becomes clear (by positive cytology and absence of growth on bacterial culture) that ascites is related to malignancy and not infection.

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- Avoid serum CA125 testing as it is often falsely elevated in the presence of ascites. In fact, virtually all patients, including men, with ascites or pleural fluid of any cause have elevated serum level of CA125. In ovarian cancer, CA125 should not be used to monitor response for at least 28 days following a paracentesis.

### Prognosis

- Ascites in women with epithelial ovarian / peritoneal cancer is not necessarily associated with a severely limited prognosis – such patients will often live for years (with resolution of their ascites) once treatment of the underlying cause is established.
- When a patient develops ascites in the setting of a non-ovarian / peritoneal cancer, the prognosis is usually poor and often less than three months. Paracentesis here is symptom-driven with the focus on improving quality of life.

## Treatment

### Treatment of underlying cause

- For women with a new diagnosis of epithelial ovarian / peritoneal cancer, the initial treatment of choice is surgical debulking with chemotherapy. More than one-half of these patients will have a complete remission from this treatment.
- For other solid tumours with malignant ascites, prognosis is poor and the role of surgery is not established. Palliative systemic therapy is sometimes appropriate, with the specific regimen chosen based upon the primary site of cancer.

### Paracentesis

- Abdominal paracentesis with appropriate ascitic fluid analysis is the most efficient way to confirm the presence of ascites, diagnose its cause, and determine if ascitic fluid is infected.
- Paracentesis is the mainstay of treatment for peritoneal carcinomatosis other than that caused by epithelial ovarian / peritoneal cancers. With these gynaecological cancers, repeated abdominal paracentesis is sometimes needed initially while chemotherapy treatment is established, with the frequency of drainage again guided by patient symptoms.
- Aim to drain 1 litre every 2 - 4 hours until dry, clamping the drain in between. Large volumes of fluid can usually be removed without fear of haemodynamic sequelae or circulatory failure. Available data suggests colloid / albumin replacement to prevent haemodynamic deterioration after paracentesis is not necessary. Remove drains after 48 hours. If patients require very frequent drainage for symptom control then consider an indwelling drain. Ascitic fluid will be bloody in about 20% of malignancy-related ascites.
- Patients often have a poor appetite and thus a diet should be considered to maximise caloric intake.

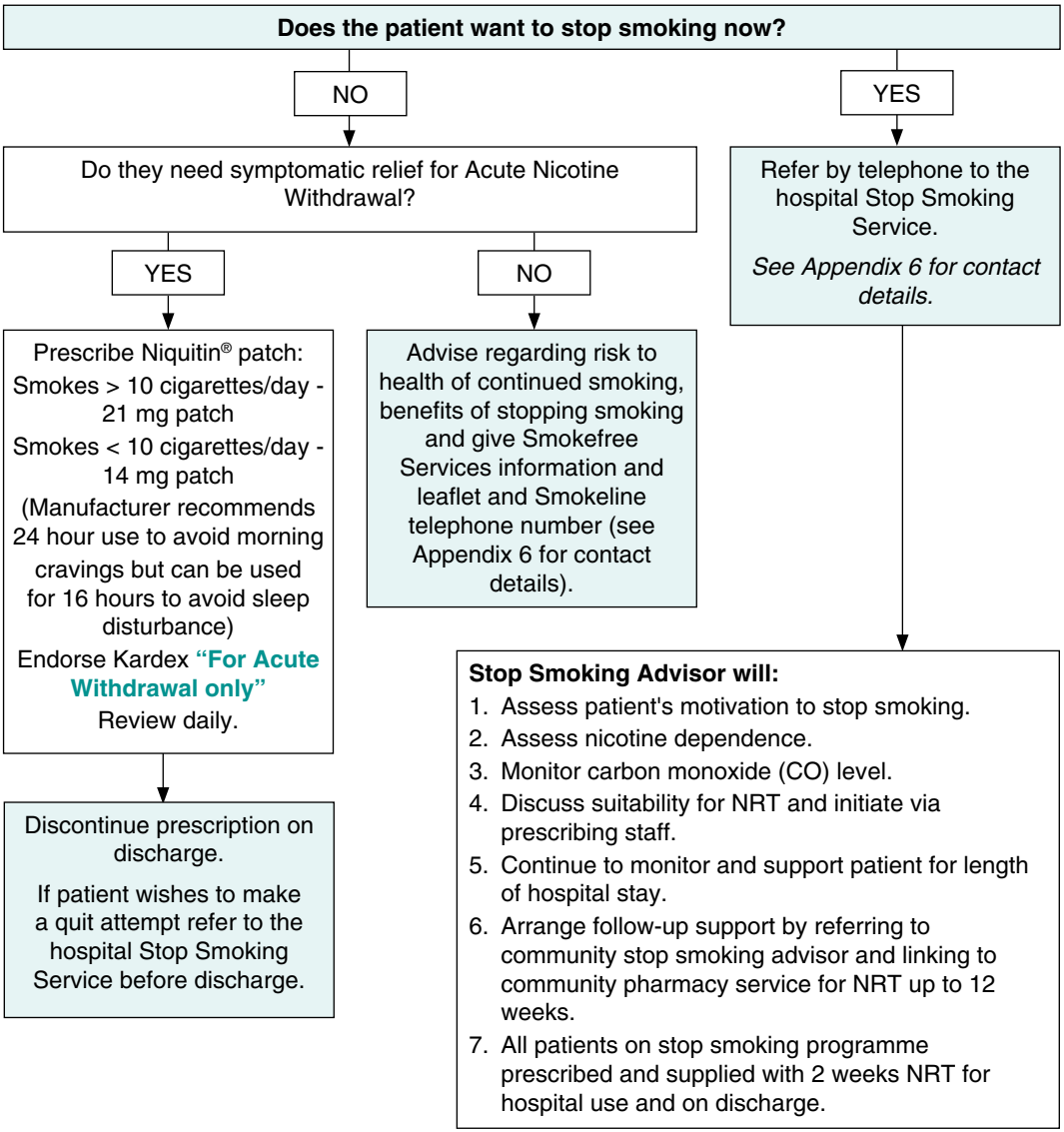
### Diuretics

- Consider if there is peripheral oedema or refractory ascites. They are more likely to be effective if portal hypertension is contributing to the pathophysiology of the ascites.
- Commence **Spironolactone oral 100mg daily** (initial dose), and titrate upwards as necessary. Closely monitor U&Es with GP support as necessary. Furosemide can be considered as an alternative if hyperkalaemia develops.

# Appendices

# Appendix 1

# Nicotine Replacement Therapy (NRT)




**N.B.** All pregnant women should be referred to NHSGGC Smokefree Pregnancy Services. See Appendix 6 for contact details.

# Appendix 2

# Preparation of Intravenous Medicines

The UK NHS Injectable Medicines Guide (IMG) (Medusa) is an electronic resource containing information on the IV preparation and administration of over 200 injectable medicines. In each clinical area a folder containing 83 core monographs is available (entitled NHSGGC Adult Intravenous Medicine Monographs) with further monographs available via StaffNet or www.injguide.nhs.uk (username and password available on StaffNet). The monographs available on Medusa are not exhaustive.

It should be noted that monographs will not be available for every drug and it may be necessary to refer to other sources of information for advice on preparation and administration such as:

- Summary of Product Characteristics (SPC) for the medicine (usually available at: www.medicines.org.uk)
- BNF www.bnf.org/bnf/index.htm or www.knowledge.scot.nhs.uk (password required)
- Medicines Information Centres – see Appendix 6 for contact details.

Specific information regarding intravenous dosing for the following medicines are included in this section:

- Aminophylline
- Amiodarone
- Glyceryl trinitrate (GTN)

**N.B.** Dobutamine and Dopamine dosing information is no longer detailed in this handbook. Refer to local protocols as practice between sites may differ.

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## Aminophylline

If intravenous aminophylline is required in a patient who was already taking a theophylline preparation, check the serum theophylline concentration and seek advice before giving a loading dose. If an infusion is required, monitor the patient closely for adverse effects and check the concentration within 24 hours. Contact your clinical pharmacist or Medicines Information for further advice.

| Aminophylline | Loading dose | Maintenance infusion |
|---|---|---|
| Dose | 5 mg/kg | 0.5 mg/kg/hr |
| Preparation | Add dose to<br>100 ml glucose 5%<br>or sodium chloride 0.9% | Add 500 mg (20 ml) to<br>500 ml glucose 5%<br>or sodium chloride 0.9% |
| Weight (kg) | Dose (volume)<br>of 250 mg / 10 ml ampoule | Infusion rate |
| 40 | 200 mg (8 ml) | 20 ml/hr |
| 50 | 250 mg (10 ml) | 25 ml/hr |
| 60 | 300 mg (12 ml) | 30 ml/hr |
| 70 | 350 mg (14 ml) | 35 ml/hr |
| 80 | 400 mg (16 ml) | 40 ml/hr |
| 90 | 450 mg (18 ml) | 45 ml/hr |
| 100 | 500 mg (20 ml) | 50 ml/hr |
| Other | Dose (mg) = 5 x wt (kg)<br>Vol (ml) = (dose/250) x 10<br>Maximum 500 mg (20 ml) | 0.5 x wt (kg) = ml/hr |
| Infusion rate | 300 ml/hr (over 20 minutes) | Up to 50 ml/hr |

## Amiodarone

Give amiodarone through a central line. If this is not feasible, give the drug through as large a vein as possible (for example median cubital) or via a suitable long line, inserted peripherally.

| Amiodarone | Loading Dose | Infusion 1 | Infusion 2 |
|---|---|---|---|
| Dose | 300 mg<br>over 1 hour | 450 mg<br>over 12 hours | 450 mg<br>over 12 hours |
| Preparation | Add 300 mg (6 ml)<br>to 250 ml glucose 5% | Add 450 mg (9 ml)<br>to 250 ml glucose 5% | Add 450 mg (9 ml)<br>to 250 ml glucose 5% |
| Infusion rate | 250 ml/hr<br>for 1 hour | 21 ml/hr<br>for 12 hours | 21 ml/hr<br>for 12 hours |

### Glyceryl Trinitrate (GTN) infusion

| GTN Dose | Normotensive patient<br>1 mg/hour | Hypotensive patient<br>0.5 mg/hour |
|---|---|---|
| Preparation<br>(Use 5 mg/ml ampoule) | Add 50 mg (10 ml) to 500 ml polyfusor of glucose 5% or sodium chloride 0.9% | Add 50 mg (10 ml) to 500 ml polyfusor of glucose 5% or sodium chloride 0.9% |
| Infusion Rate | 10 ml/hour<br>Increasing according to clinical response | 5 ml/hour<br>Increasing according to clinical response |

### Glyceryl Trinitrate (GTN) syringe driver (50 mg / 50 ml)

| | |
|---|---|
| Preparation | Draw up 50 mg (50 ml) GTN into a 50 ml BD Plastipak syringe.<br>No need for further dilution. |
| Infusion Rate | Normotensive patient: 1 ml/hour (1 mg/hour)<br>Hypotensive patient: 0.5 ml/hour (0.5 mg/hour)<br>Further increases should be based on clinical response |

- Extravasation may cause tissue damage.

# Appendix 3

## Therapeutic Drug Monitoring (target concentration ranges)

**Table 1 – Antibiotics**

| Drug | Time to steady state | Ideal sampling time | Target Range | Comments |
|---|---|---|---|---|
| Amikacin | 1 day (longer in renal impairment) | Trough End of dose interval<br><br>Peak 1 hr after dose | < 5 mg/L (< 2 mg/L for alternative dosing guidelines)<br>15 - 30 mg/L (> 35 mg/L for alternative dosing guidelines) | Dose depends on renal function (see page 261) |
| Gentamicin | 1 day (longer in renal impairment) | 6 - 14 hrs after dose | See plot on page 264 | Dose depends on renal function (see page 262) Peak 1 hr post dose > 10 mg/L and trough < 1 mg/L |
| Tobramycin | 1 day (longer in renal impairment) | Trough End of dose interval<br><br>Peak 1 hr after dose<br><br>OR<br>6 - 14 hrs post dose (if not CF) | <1 mg/L<br><br>>10 mg/L<br><br>Use gentamicin plot on page 264 | Use patient specific dose in cystic fibrosis (CF)<br><br>Use gentamicin guidelines if patient specific dose is not available |
| Vancomycin | 1 day (longer in renal impairment) | Trough End of dose interval<br><br>During constant rate infusion | 10 - 20 mg/L<br><br>15 - 25 mg/L | Page 266 - 269<br><br>Page 270 - 272 |

For further advice on when to take blood samples and how to interpret the results please contact your clinical pharmacist.

**Table 2 – Other drugs**

| Drug | Time to steady state | Ideal sampling time | Target Range | Comments |
|---|---|---|---|---|
| Carbamazepine | 2 - 3 weeks (new therapy)<br>2 - 4 days (dose change) | Predose (not critical) | 4 - 12 mg/L | Metabolised in the liver, autoinduction |
| Ciclosporin | 2 - 4 days | Predose | Depends on use and time post transplant | Metabolised in the liver |
| Digoxin | 7 - 10 days | 6 - 24 hours after dose | 0.5 - 2 micrograms/L<br>0.5 - 1 micrograms/L in heart failure | Dose depends on renal function |
| Lithium | 5 days | 12 hours after dose (24 hourly dosing) | 0.4 - 1 mmol/L | Dose depends on renal function |
| Phenytoin | 2 - 3 weeks | Predose (not critical) | 10 - 20 mg/L | Metabolised in the liver.<br>5 - 10 mg/L may be adequate.<br>Seek advice if albumin < 32 g/L. |
| Tacrolimus | 2 - 4 days | Predose | Depends on use and time post transplant | Metabolised in the liver |
| Theophylline | 2 - 3 days | 8 - 12 hours after dose (not critical) | 10 - 20 mg/L | Metabolised in the liver.<br>5-10 mg/L adequate |
| Valproic acid | 3 days | Predose | 50 - 100 mg/L | Metabolised in the liver. Analysis rarely useful. |

For further advice on when to take blood samples and how to interpret the results please contact your clinical pharmacist.

**N.B.** Interactions are common with these drugs – see BNF Appendix 1 or contact your clinical pharmacist for details.

# Appendix 4

# Mental Health Legislation relating to Emergency Sedation

In medical and psychiatric emergencies for any ***non detained*** patient, common law allows treatment to protect patient's life and/or wellbeing and/or wellbeing of others. No certification is needed beyond description of the action in the casefile. However any patient who has capacity to make or withhold consent cannot be given medical treatment without that consent. The law provides the remedies below for the treatment of patients incapable to consent to treatment because of mental disorder. Advice can be sought within working hours from liaison psychiatry in the general hospitals and outwith working hours from the duty psychiatrists at local psychiatric hospitals (see Appendix 6 for contact numbers).

## Adults with Incapacity (Scotland) Act 2000

A patient who is incapable of making decisions about medical treatment can be given "any procedure or treatment designed to safeguard or promote physical or mental health" under section 47 of the Adults with Incapacity (Scotland) Act 2000 in the absence of consent, subject to the principles of that Act. This requires the 'medical practitioner primarily responsible for the medical treatment of the adult i.e. usually their medical / surgical Consultant or General Practitioner to issue a section 47 Certificate of Incapacity.

## Mental Health (Care and Treatment) (Scotland) Act 2003

The Act allows for the administration of medication to treat mental disorder (includes acute disturbed behaviour secondary to delirium and dementia) without and/or against consent of patient. It does not allow administration of non psychiatric treatments without consent.

In medical emergencies for any ***detained patient***, section 243, Mental Health (Care & Treatment) (Scotland) Act 2003 allows the administration of medical treatment, without consent to:

- Save the patient's life
- Prevent serious deterioration in the patient's condition
- Alleviate serious suffering on the part of the patient
- Prevent the patient behaving violently and/or being a danger to themselves or others.

Following this treatment the administering doctor has a responsibility to inform the Mental Welfare Commission of their action ***within 7 days*** and to inform the patient's Responsible Medical Officer.

# Appendix 5

# Normal Immunoglobulins

Normal immunoglobulins are plasma products that remain the only treatment option for patients with primary immunodeficiencies which, in certain cases, are life-threatening. These medicines are prone to temporary shortages and it is imperative to minimise the impact of these shortages by limiting their use to patients who have a clear indication for treatment. In addition, normal immunoglobulins represent a significant cost pressure for NHSGGC.

Considering the above, the use of normal immunoglobulins is restricted to specific indications and treatment must be initiated and reviewed by a Consultant.

## Red indications: High priority

Treatment may be life-saving. Supply should be reserved for these indications in time of shortage.

## Blue indications: Medium priority

Evidence base is reasonable but other treatment options are available. Treatment should be modified in times of shortage.

## Grey indications: Low priority (non-Formulary)

Evidence base is weak, in many cases because the disease is rare. Treatment should be considered on a case by case basis, prioritised against other competing demands.

## Black indications: Use is not appropriate (non-Formulary)

The prescription of normal immunoglobulins *is not recommended* for these conditions

A comprehensive list of colour-coded indications can be found on the National Guidelines for the Use of Normal Immunoglobulins for NHS Scotland. An updated version of these guidelines has been issued in March 2012 and is available as a pdf on www.nsd.scot.nhs.uk (select Publications, Guidelines and Other Reports, then Guidelines Section) or on StaffNet, Clinical guideline electronic resource directory and search in 'Haematology section'. Treatment with normal immunoglobulins for grey or black indications is considered non-Formulary within NHSGGC. Any indication not listed in the National Guidelines is also non-Formulary. Requests for these indications should follow non-Formulary standard procedures.

Normal immunoglobins should be prescribed generically with the exception of patients with primary immunodeficiency and those on home therapy. Any contraindications / allergies to specific brands must be made on the request form *and on the drug kardex*. For the dosing calculation of intravenous normal immunoglobulins in overweight patients, follow recommendations available on StaffNet, Clinical Guidelines Electronic Resource Directory and search under 'Haematology'. Information on administration and monitoring parameters during infusion is also available on the same location on StaffNet.

The ordering process for these medicines is currently under review. At the time of writing ordering remains based on specific paper documentation which is available from Pharmacy upon request and must be completed prior to supply. Relevant staff will be notified of changes to the ordering process in due course. Contact your local Pharmacy department (see Appendix 6 for contact details) if you require further information on this.

# Appendix 6

# Useful telephone numbers

**N.B.** Only in the Glasgow hospitals are the phone extensions active between sites.

### Allergy Service

West of Scotland Anaphylaxis Service (Western Infirmary) .....0141 211 1823

### Antimicrobial Management Team (AMT)

Lead Physician .....0141 211 0292 or 50292

Lead Microbiologist .....0141 211 4640 / 4651

Lead Pharmacist .....0141 211 3000, page 5271 or ext 57963

Antimicrobial Pharmacists

Gartnavel General, Western Infirmary, and Beatson.....0141 211 3322 or 53322 or page 5008

Glasgow Royal Infirmary and Stobhill.....0141 211 4775 or 24775 or page 3997

Inverclyde Royal.....01475 633777 ext 64070

Southern General and Victoria Infirmary .....0141 201 5533 or 65533 or page 6055

Royal Alexandra and Vale of Leven .....01389 817 571 or page 56260 via RAH switchboard

Royal Hospital for Sick Children (Yorkhill).....0141 201 0680 or 80680 or page 8198

For microbiology, see page 351.

For Renal pharmacist, look under Western Infirmary.

### Beatson WOSCC

0141 301 7000

Medicines Information .....24407 (GRI)

Pharmacy dispensary.....0141 301 7409

### Brownlee Centre (at Gartnavel General)

Duty page .....0141 211 3000, page 5295

HIV pharmacist (during work hours).....0141 211 3000, page 5388

*Continues on next page*

## Drug Misuse

### Hospital Liaison Addiction Nurse Service

Southern General / Victoria Infirmary / Gartnavel General / Glasgow Royal Infirmary / Western Infirmary / Stobhill.....0141 418 4942 / 4943

### Glasgow Addiction Services

Main switchboard.....0141 276 6600

Glasgow Addiction Services Senior Medical Officers.....0141 276 6600

### Renfrewshire Drug Service

Main switchboard .....0141 889 1223

### Inverclyde Drug Service

Main switchboard .....01475 502 344

### Leven Addiction Services

Main switchboard.....01389 812 018

### Clyde Special Needs In Pregnancy Service (SNIPS)

Royal Alexandra .....0141 314 6199

Inverclyde Royal .....01475 504 833

Vale of Leven.....01389 817 270

### Clyde Doctors

Ravenscraig.....01475 633 777

Dykebar .....0141 884 5122

Leven Addiction Services .....01389 812 018

### Pregnancy Services in Glasgow

Women's Reproductive Health Service (telephone: Main switchboard - 0141 211 5400 and ask to radio page Dr Hepburn, or Dr Ellis, or the WRHS on call midwife) or SNIPs in Clyde.

Glasgow Addiction Services Pharmacy Team.....0141 276 6600

## Formulary Team

0141 211 4407

## Gartnavel General Hospital

0141 211 3000

Medicines Information .....24407 (GRI)

On-call GU Medicine Doctor.....page via switchboard

Pharmacy dispensary.....53316

*Continues on next page*

**Glasgow Royal Infirmary (GRI)**

0141 211 4000

Medicines Information .....24407

Pharmacy dispensary .....25004

**Glasgow and Clyde Anticoagulation Service (GCAS)**

0141 232 0800

Lead Nurse for the Glasgow and Clyde Anticoagulant Service .....0141 211 8731

Anticoagulation pharmacist ..... 01389 754121 pager 53092 (or via pharmacy, Vale of Leven)

**Golden Jubilee National Hospital**

0141 951 5000

**Inverclyde Royal Hospital**

01475 633 777

Medicines Information .....0141 314 6819 (RAH)

Pharmacy dispensary .....65421

**Liaison Psychiatrists**

*During work hours*

Glasgow Royal Infirmary (East Team).....0141 211 4417 or 24417

Ravenscraig .....01475 633 777 (IRH switchboard)

Southern General (South Team) .....0141 201 2422 or 62422

Stobhill (North Team) .....0141 531 3255 or 43255

Vale of Leven Hospital.....01389 817 572 (Christie Ward)

Western Infirmary (West Team) .....0141 211 2131 or 52131

*Out-of-hours*

Dykebar .....0141 314 4000

Gartnavel Royal.....0141 211 3600

Leverndale .....0141 211 6400

Parkhead .....0141 211 8300

Ravenscraig .....01475 633 777 (IRH switchboard)

Southern General ..... 0141 201 1100

Stobhill .....0141 531 3100

Vale of Leven .....01389 754 121 (Christie Ward)

**Liver Transplant Unit**

(Edinburgh Royal Infirmary) .....0131 242 2068 / 2069

*Continues on next page*

### Outpatient Parenteral Antibiotic Therapy (OPAT)

During work hours ..... 0141 211 1053
or extension 51053
or 0141 211 3000, and radiopage
07939585652

Out of working hours
(Brownlee Centre) ..... 0141 211 3000, page 5295

### Medicines Information *See under individual hospital*

### Microbiology contact numbers during working hours

Southern General ..... page 7077

Victoria Infirmary ..... page 7997

Glasgow Royal / Stobhill / Western Infirmary /
Gartnavel General ..... page 3702

RAH / VoL / IRH ..... 314 6904

Out with working hours: phone switchboard and ask for the oncall microbiologist

### National Poisons Information Service (NPIS)

0844 892 0011

### Parkinson's disease nurse specialists

Drumchapel hospital ..... 0141 211 6012

Glasgow Royal and Lightburn ..... 0141 211 1522

Inverclyde Royal ..... 0141 314 6833

Royal Alexandra ..... 0141 314 6833

SGH Institute of Neurological Sciences ..... 0141 201 2590 / 2747

Southern General ..... 0141 201 2453

Stobhill ..... 0141 355 1480

Vale of Leven ..... 0141 314 6833

Victoria Infirmary..... 0141 201 6319

### Pharmacy Dispensary *See under individual hospital*

### Public Health Protection Unit (NHSGGC)

0141 201 4444

### Royal Alexandra Hospital (RAH)

0141 887 9111

Medicines Information ..... 46819

Pharmacy dispensary..... 47070

### Sandyford Centre

Sandyford Centre (Sexual Health Service)..... 0141 211 8130
or page on-call GUM via Gartnavel General switchboard

*Continues on next page*

Sandyford Initiative (GUM) .....0141 211 8130

For on-call page GU Medicine doctor – page via Gartnavel switchboard

Sandyford Initiative – Professional Helpline .....0141 211 6717

### Smoking Cessation

Smokeline.....0800 84 84 84

North Glasgow – Stop Smoking Service.....0141 232 2110 or 0141 201 9832

Clyde Hospitals – Stop Smoking Service ..... 01475 501 226

South Glasgow – Stop Smoking Service..... 0800 028 5208

Smokefree Pregnancy Services ..... 0141 201 2335

### Southern General Hospital

0141 201 1100

Medicines Information ..... 24407 (GRI)

Neurosurgical Registrar (on-call) via SGH switchboard ..... Page 7777

Pharmacy dispensary..... 61393

### Stobhill Hospital

0141 201 3000

Medicines Information ..... 24407 (GRI)

Pharmacy dispensary..... 13579

### Vale of Leven Hospital

01389 754 121

Medicines Information ..... 0141 314 6819 (RAH)

Pharmacy dispensary..... 27540

### Victoria Infirmary

0141 201 6000

Medicines Information ..... 24407 (GRI)

Pharmacy dispensary..... 65549 / 65594

### Western Infirmary

0141 211 2000

Medicines Information ..... 24407 (GRI)

Pharmacy dispensary..... 52386

Renal pharmacist ..... 0141 211 1845 or 51845
or radio page 07659 535860

### Women's Reproductive Health Service (WRHS)

0141 211 5400 (ask for radiopage of Dr Hepburn, Dr Ellis or the on-call WRHS Midwife)

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